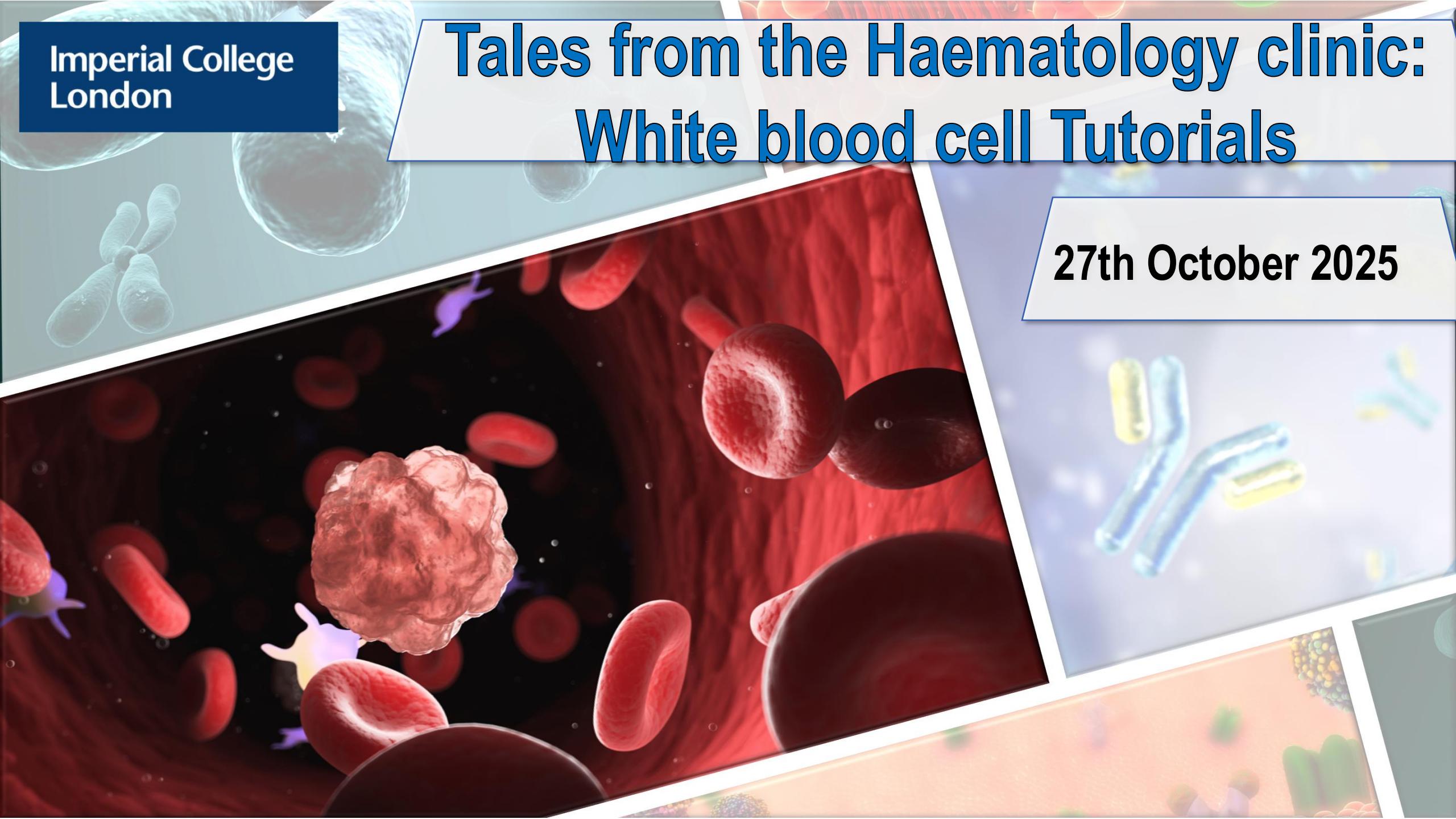


Tales from the Haematology clinic: White blood cell Tutorials

27th October 2025





Session Plan

Part 1 – Discussion of 6 cases

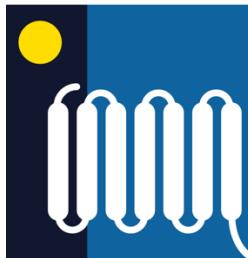
- 6 **interactive** cases
- The cases are of patients with abnormalities of different types of white blood cell
- They illustrate important principles

Part 2 – Summary

- A 5 - 10 minute discussion at the end will bring it all together

Part 3 – Consolidation

- Post session Reading: Leukaemia - on Insendi
- ‘Test yourself’ Activity - on Insendi
- **Answers to Tutorial Questions will be available on Insendi at 1500 h on 27th October 2025**



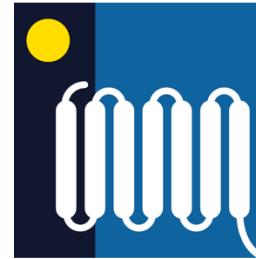
Case 1

- A 32-year-old man presents to his GP with progressive breathlessness, chest pain and a cough that is productive of green sputum over the previous few days
- He has a history of asthma for which he intermittently uses inhalers
- On examination he is noted to have a raised temperature, a widespread wheeze and a few coarse crackles at the left lung base; examination is otherwise unremarkable
- The GP performs a Full Blood Count (FBC)

Q.1 What abnormalities are shown on the Full Blood Count?

	Value	Normal Range
Hb (g/l)	150 g/l	133-167
MCV (fl)	90 fl	82-98
White cell count	$19.0 \times 10^9/l$	4.2 – 11.2
Neutrophils	$14.0 \times 10^9/l$	0.2 – 7.0
Lymphocytes	$3.0 \times 10^9/l$	1.1 - 3.6
Monocytes	$1.0 \times 10^9/l$	0.3 – 0.9
Basophils	$0.2 \times 10^9/l$	0.0 - 0.5
Eosinophils	$0.6 \times 10^9/l$	0.0 – 0.2
Platelets	$375 \times 10^9/l$	140 - 420

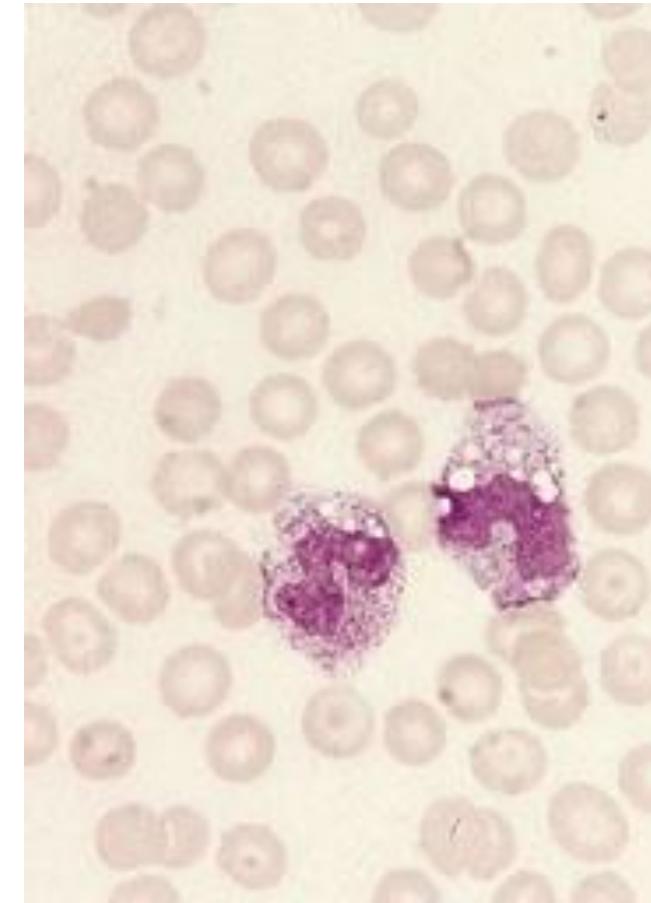
Interpreting white cells on a blood count and film: Case 1



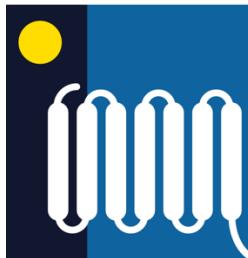
- Is there an abnormality?
- If so, which cell line is abnormal?
- Are there any clues in the clinical history?
- Are there any clues in the blood film?

Q.2 Can you think of an explanation(s) for the FBC abnormalities?

Q.3 What other tests may be helpful?

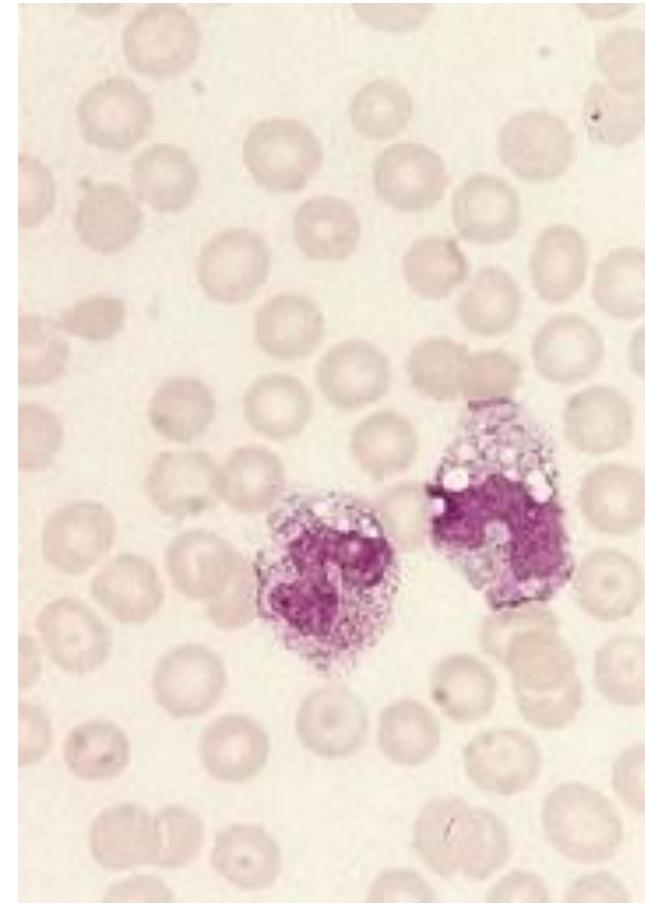


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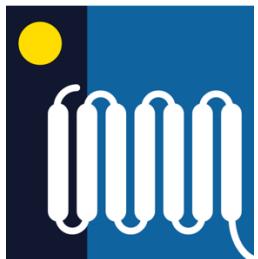


Case 1: Progress

- C Reactive Protein (CRP) raised
- Sputum sample sent for culture
- Urine antigen test
- Patient received a course of the antibiotic amoxicillin, regular steroid inhaler (beclomethasone) and bronchodilator inhaler (salbutamol)
- After one week the patient's symptoms had fully resolved



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Case 2

- A 23-year-old male medical student presents to his GP with a 1 week history of severe pharyngitis (sore throat), fever and fatigue
- On examination:
 - Tonsillar inflammation
 - Widespread palpable small lymph nodes
 - Cervical (neck)
 - Axillary (armpit)
 - Inguinal (groin)

Q.1 What abnormalities are shown on the Full Blood Count?

	Value	Normal Range
Hb (g/l)	145 g/l	133-167
MCV (fl)	90 fl	82-98
White cell count	$15 \times 10^9/l$	4.2 – 11.2
Neutrophils	$6.0 \times 10^9/l$	0.2 – 7.0
Lymphocytes	$8.0 \times 10^9/l$	1.1 - 3.6
Monocytes	$0.7 \times 10^9/l$	0.3 – 0.9
Basophils	$0.2 \times 10^9/l$	0.0 - 0.5
Eosinophils	$0.1 \times 10^9/l$	0.0 – 0.2
Platelets	$375 \times 10^9/l$	140 - 420

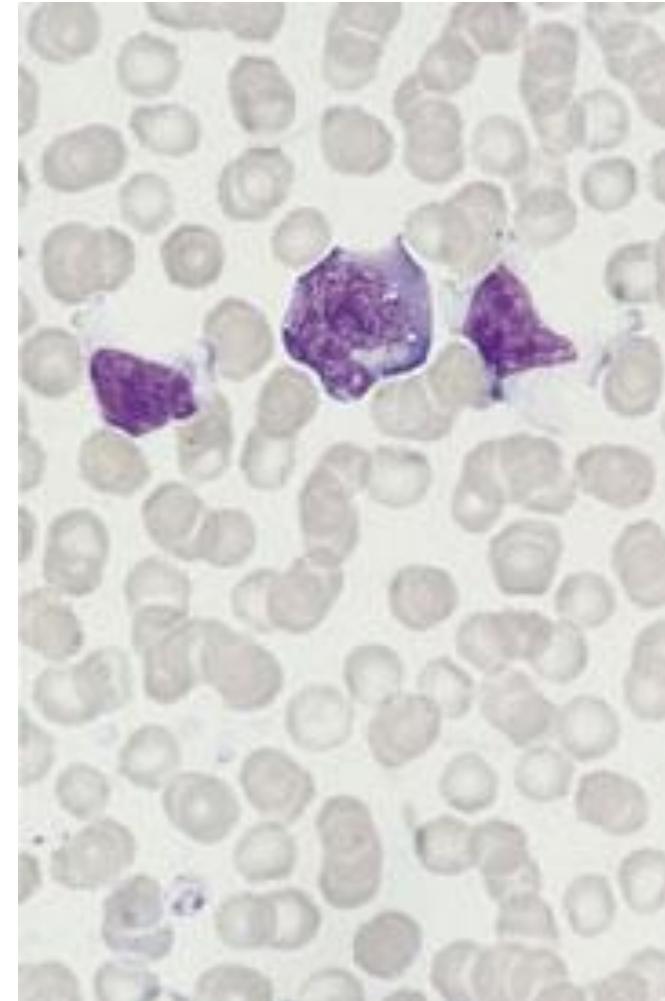
Interpreting white cells on a blood count and film: Case 2



- Is there an abnormality?
- If so, which cell line is abnormal?
- Are there any clues in the clinical history?
- Are there any clues in the blood film?

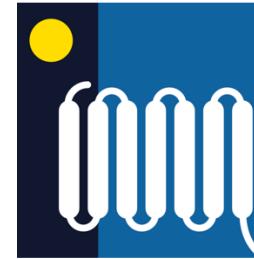
Q.2 Can you describe the appearances of these white cells?

Q.3 What do you think is the most likely cause?



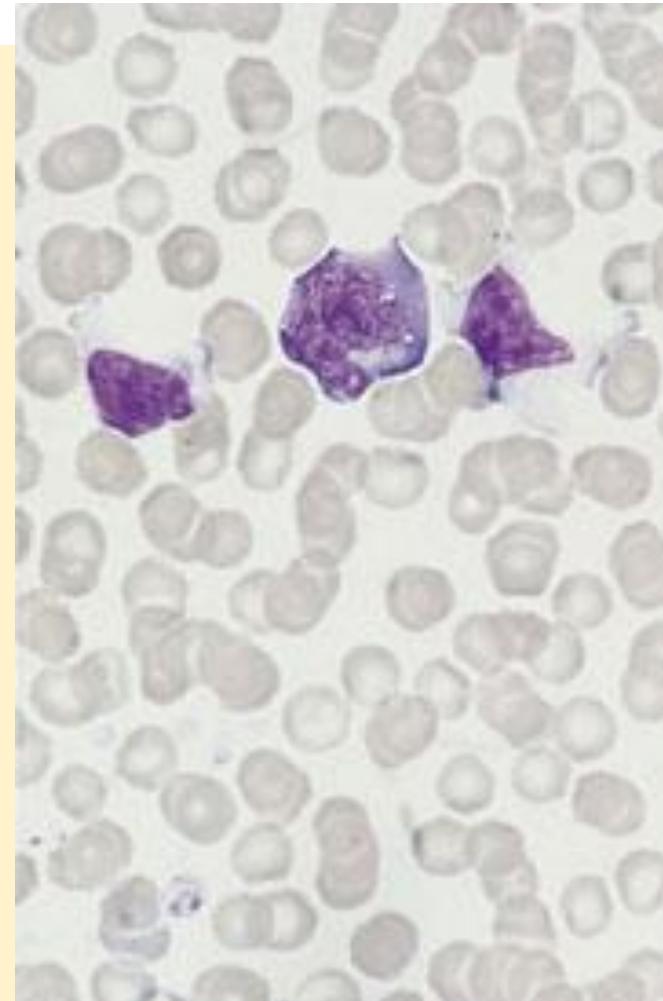
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Case 2: Infectious Mononucleosis ('glandular fever')



- When lymphocytosis is due to a viral infection there are often 'atypical lymphocytes'
- This patient's blood film shows 'atypical lymphocytes' with the following features
 - the lymphocyte in the middle is large and has intensely basophilic cytoplasm
 - the scalloped margins and 'hugging' of the surrounding red blood cells is a characteristic finding in infectious mononucleosis ('glandular fever'), resulting from Epstein–Barr virus infection

Q.4 What test would confirm this diagnosis?



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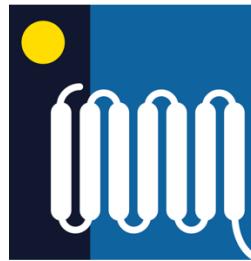
Case 3

- A 78-year-old woman who is in good general health has a routine FBC before hip surgery

Q.1 What abnormality is shown on the FBC?

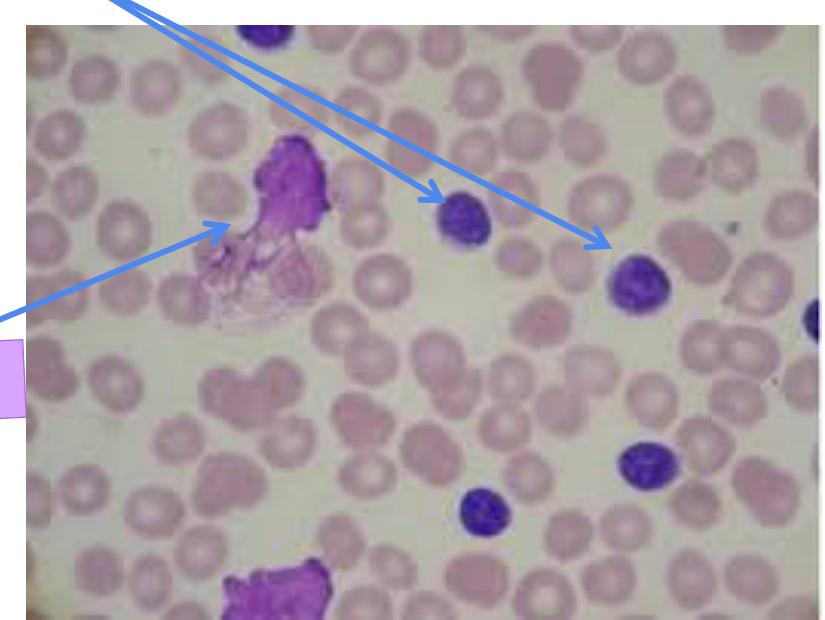
	Value	Normal Range
Hb (g/l)	120 g/l	118-148
MCV (fl)	86 fl	82-98
White cell count	$26.5 \times 10^9/l$	4.2 – 11.2
Neutrophils	$6.0 \times 10^9/l$	0.2 – 7.0
Lymphocytes	$20 \times 10^9/l$	1.1 - 3.6
Monocytes	$0.5 \times 10^9/l$	0.3 – 0.9
Basophils	$0.0 \times 10^9/l$	0.0 - 0.5
Eosinophils	$0.0 \times 10^9/l$	0.0 – 0.2
Platelets	$180 \times 10^9/l$	140 - 420

Interpreting white cells on a blood count and film: Case 3



- Is there an abnormality?
- If so, which cell line is abnormal?
- Are there any clues in the clinical history?
- Are there any clues in the blood film?

Q.2 What are these cells?

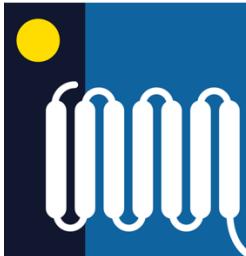


Q.3 What is this cell?

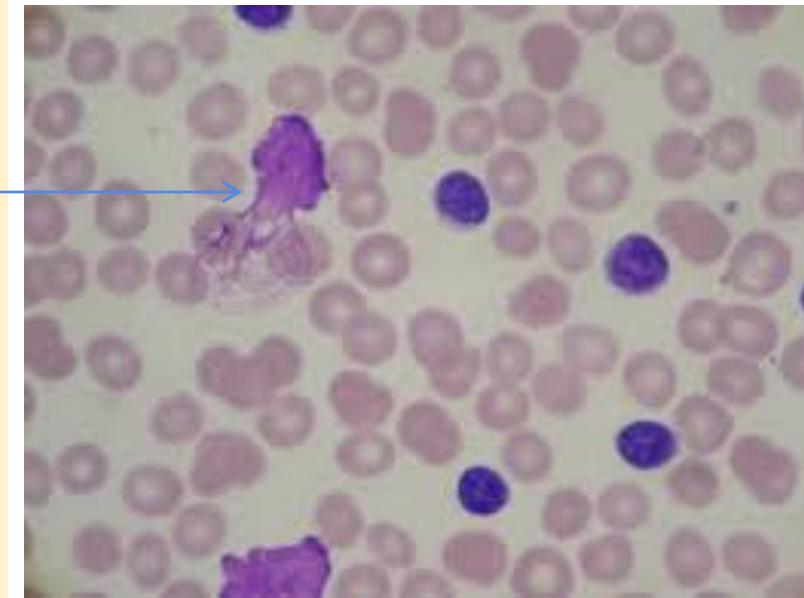
Q.4 What do you think is the most likely diagnosis?

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Case 3: Chronic Lymphocytic leukaemia (CLL)



- You can see 4 mature CLL lymphocytes
 - and a squashed CLL lymphocyte known as a 'smear' or 'smudge' cell: characteristic of CLL
- CLL is a **lymphoproliferative** disorder
- CLL is the **most common cause of persistent lymphocytosis in the elderly**
- Characterising the profile of cell surface markers expressed by lymphocytes using flow cytometry helps confirm the diagnosis
- CLL is staged according to the degree of lymph node/liver/spleen involvement, and whether Hb and platelet count are reduced (in more advanced disease)

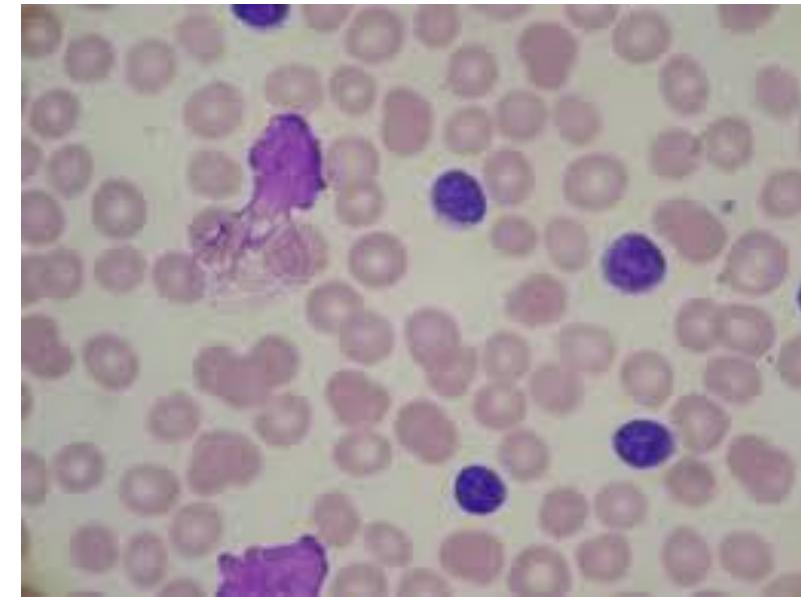


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Case 3: Progress

- On examination in the haematology clinic there are a few small superficial lymph nodes palpable
- The hip surgery proceeds uneventfully
- You advise her that she may be at increased risk of infection, often sinus or pulmonary
- She attends the clinic every 6 months for observation and FBC monitoring. Approximately 2/3 of patients will progress and ultimately require CLL directed treatment.



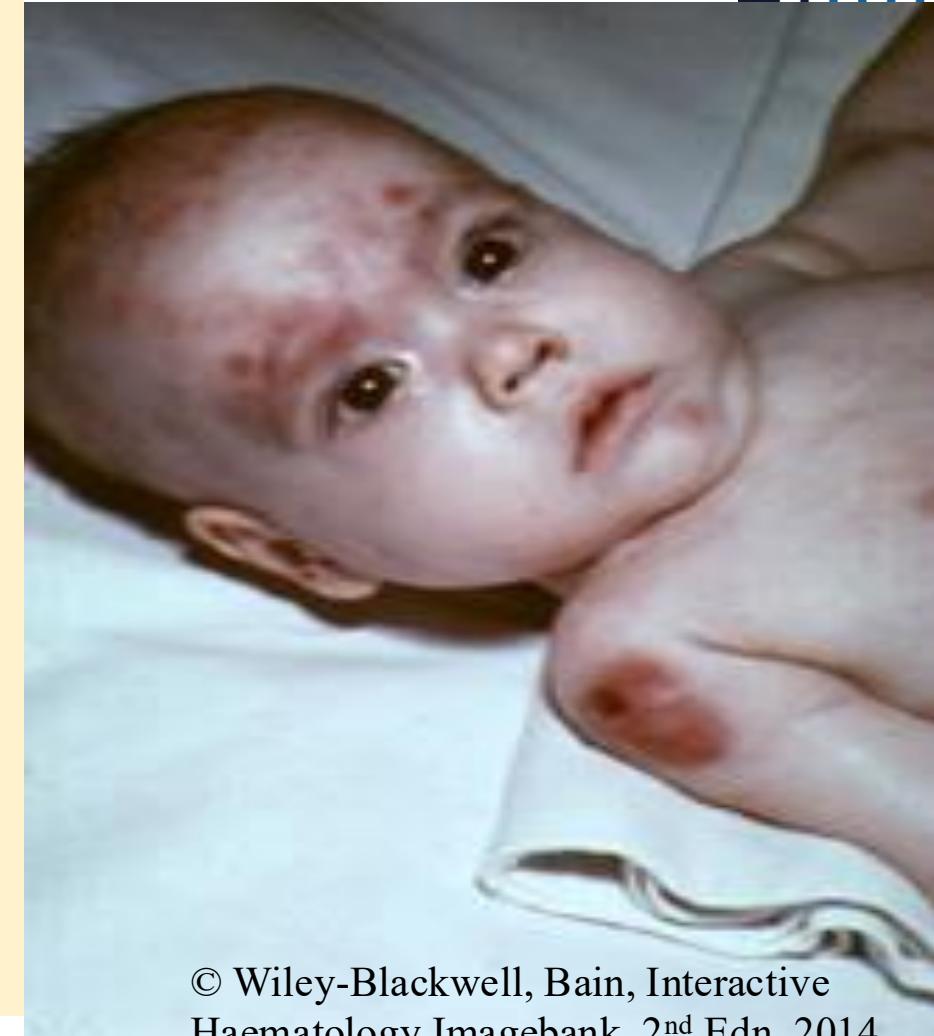
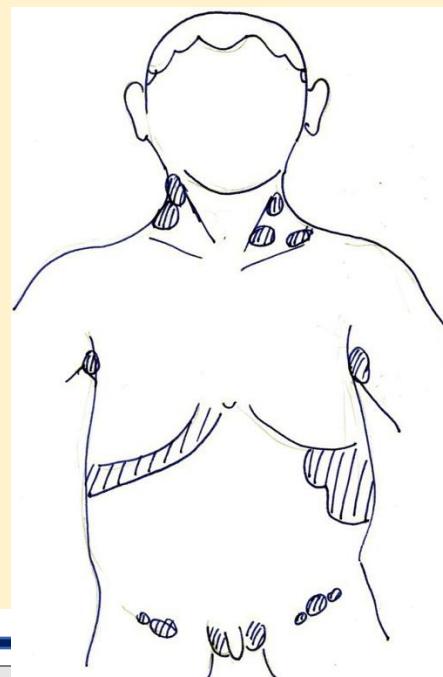
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Case 4

- A 10-month-old boy is brought into A&E by his parents with symptoms of listlessness over the past 2-3 days and evolving bruising
- On examination he is febrile, pale, & with widespread bruising
- You draw a diagram to show your examination findings

Q.1 Can you name the clinical signs shown on the drawing?



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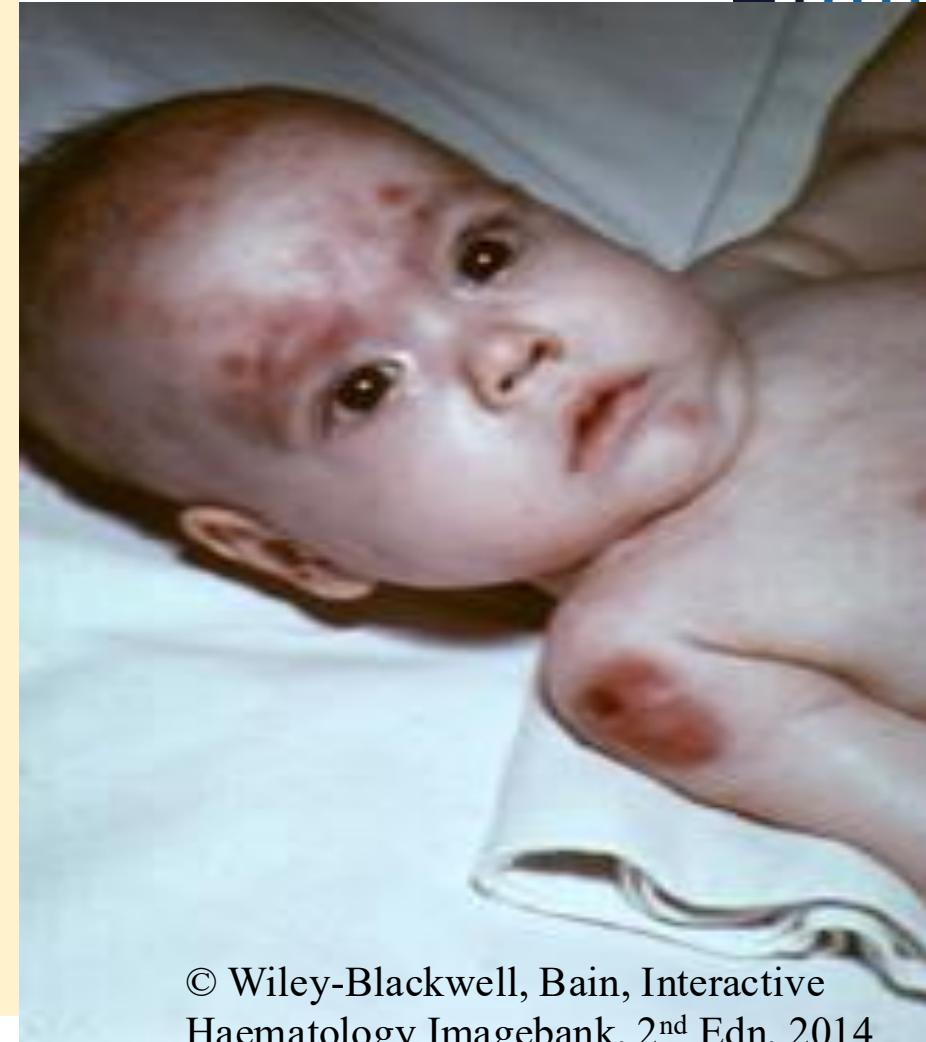
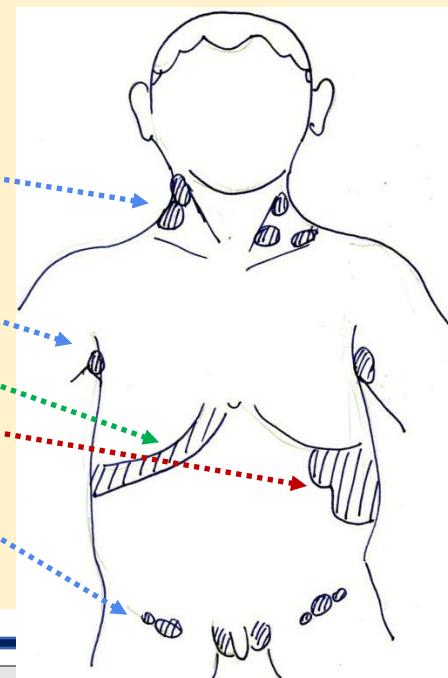
Case 4

- A 10-month-old boy is brought into A&E by his parents with symptoms of listlessness and widespread bruising over the past 2-3 days
- On examination he febrile, pale & with widespread bruising

- lymphadenopathy:

- neck/cervical
- axillae
- groin

- enlarged liver (**hepatomegaly**)
- enlarged spleen (**splenomegaly**)
- testicular swelling



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Case 4

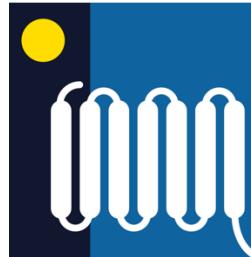
- A 10-month-old boy is brought into A&E by his parents with symptoms of listlessness and widespread bruising over the past 2-3 days
- An urgent Full Blood Count is performed:

	Value	Normal Range	
Hb (g/l)	75 g/l	115 - 148	
MCV (fl)	85 fl	82-98	
White cell count	$82 \times 10^9/l$	4.2 – 11.2	
No differential available	Film flagged as showing blasts	Q.2 What abnormalities are shown on the Full Blood Count?	
Platelets	$21 \times 10^9/l$	140-420	

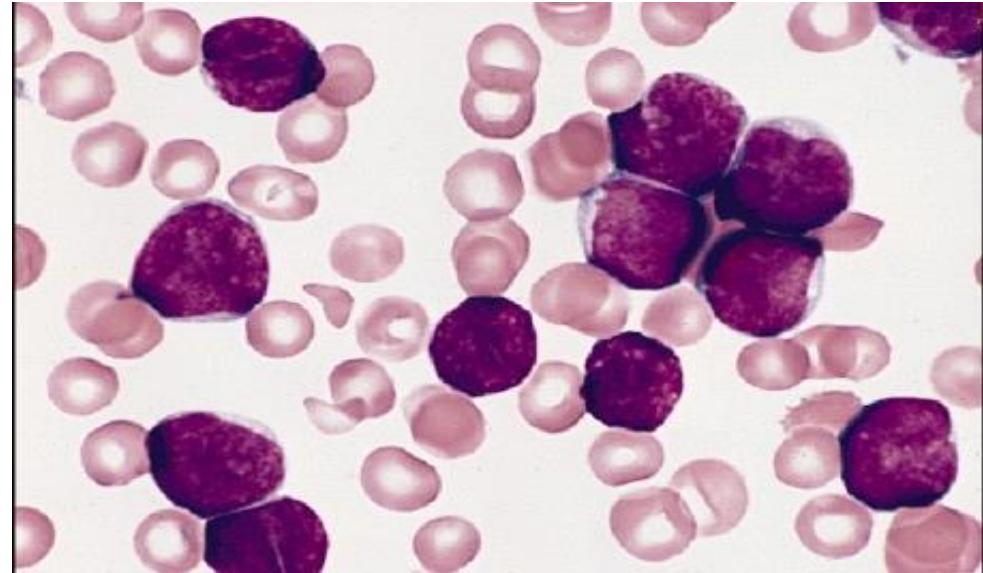


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Interpreting white cells on a blood count and film: Case 4



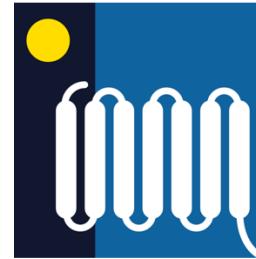
- Is there an abnormality?
- If so, which cell line is abnormal?
- Are there any clues in the clinical history?
- Are there any clues in the blood film?



www.pathology.vcu.edu

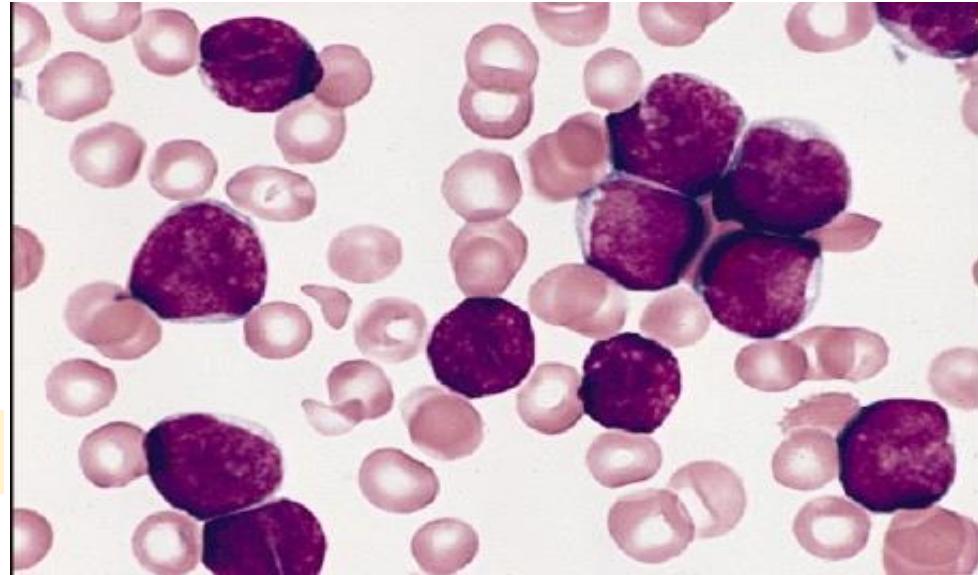
Q.3 What abnormalities can you see on the blood film?

Interpreting white cells on a blood count and film: Case 4



- Leukocytosis with lymphoblasts circulating in the blood
- Anaemia (normocytic, normochromic)
- Neutropenia
- Thrombocytopenia (low platelet count)

Q.4 How do these findings explain the clinical symptoms and signs found on examination?



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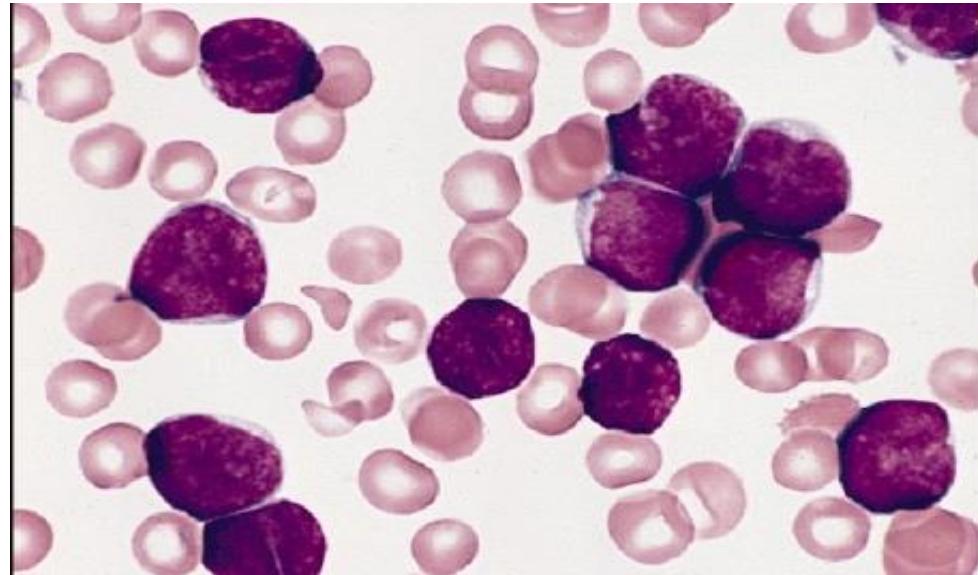
Blast cells can be recognised by:

- large size,
- high nucleus/cytoplasmic ratio
- open chromatin pattern of nuclei
- prominent nucleoli

Interpreting white cells on a blood count and film: Case 4



- Leukocytosis with lymphoblasts circulating in the blood:
 - lymphadenopathy, hepatomegaly, splenomegaly, testicular swelling
- Anaemia (normocytic, normochromic)
 - pale, lethargic/listless
- Neutropenia
 - fever
- Thrombocytopenia (low platelet count)
 - bruising/bleeding



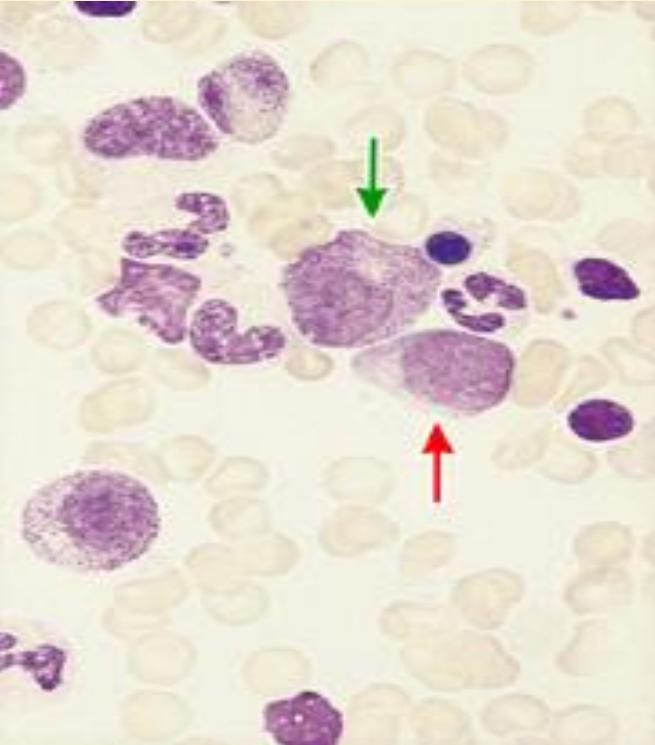
www.pathology.vcu.edu

Q.5 What is the likely diagnosis?

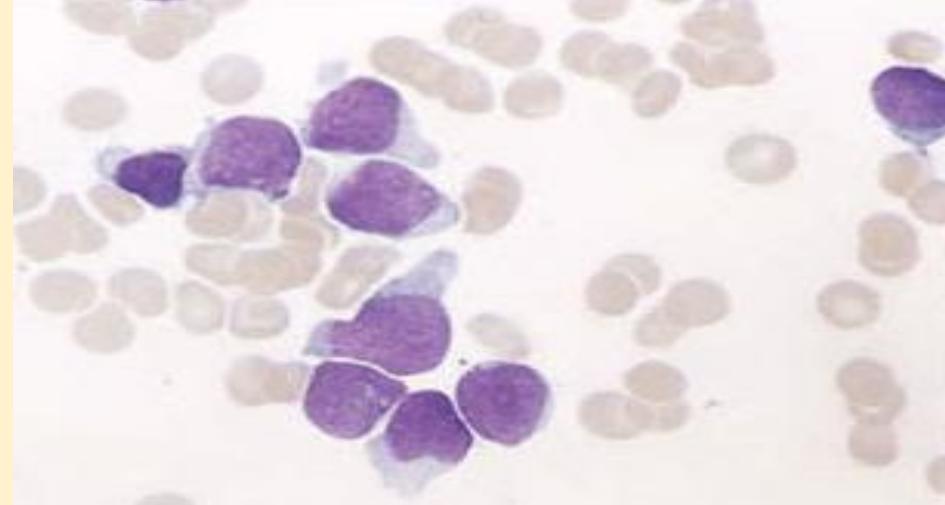
Q.6 What test(s) may provide further information?

Case 4: Acute Lymphoblastic Leukaemia (ALL)

Bone Marrow Test (Aspirate)



Normal bone marrow aspirate

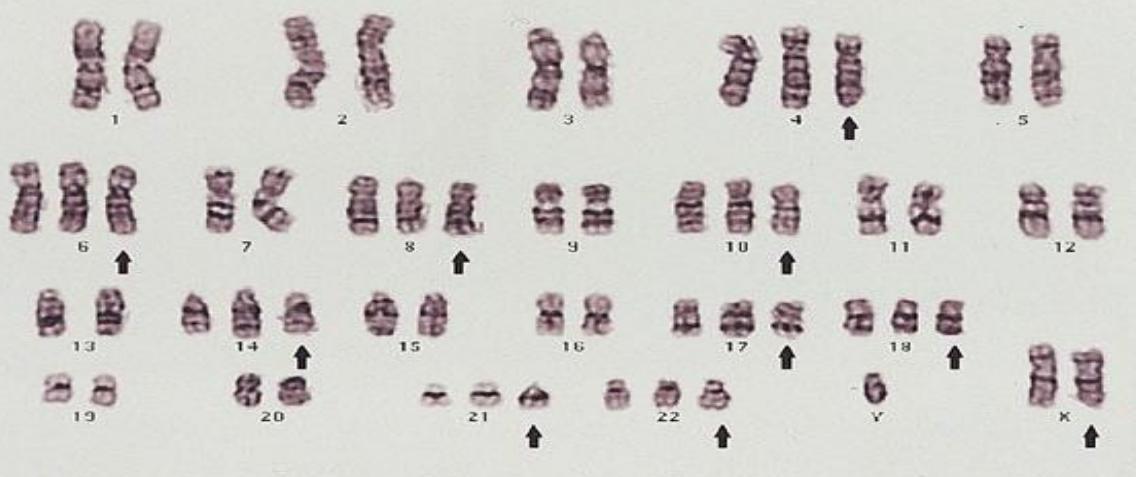


Bone marrow aspirate showing replacement of normal bone marrow cells by lymphoblasts

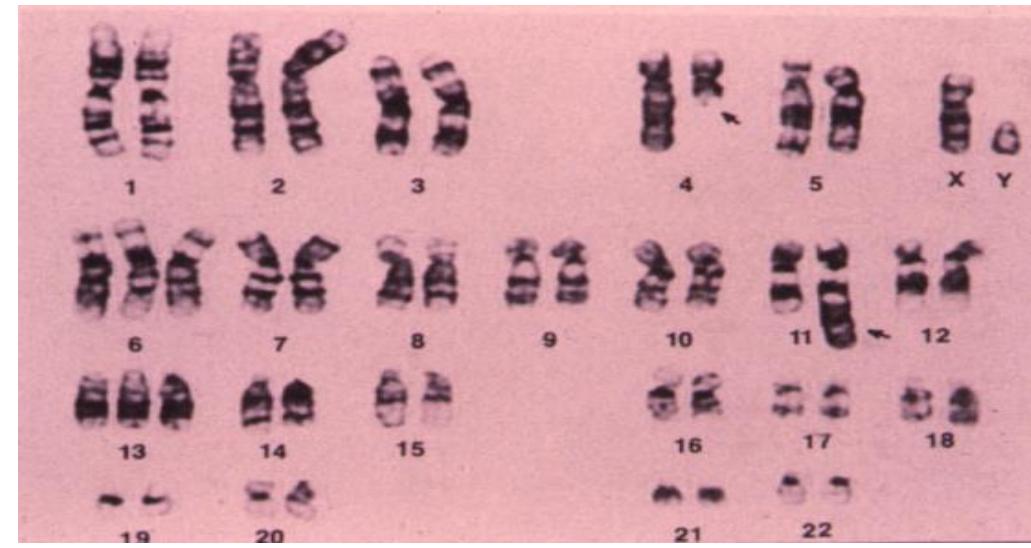
The lymphoblasts can be further characterised by assessing the profile of their cell surface e.g. using flow cytometry

Acute Lymphoblastic Leukaemia: cytogenetic and molecular genetic analysis

- Cytogenetic/molecular genetic analysis is useful for managing the individual patient because it gives us information about prognosis
- Cytogenetic/molecular genetic analysis advances knowledge of leukaemia because it has permitted the discovery of leukaemogenic mechanisms and the development of targeted treatment

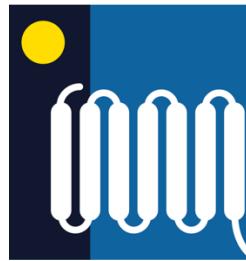


Hyperdiploidy—good prognosis



t(4;11)—poor prognosis

Acute Lymphoblastic Leukaemia: approaches to treatment



- Supportive
 - Red cells
 - Platelets
 - Antibiotics
- Systemic chemotherapy
- Intrathecal (around the spinal cord) chemotherapy

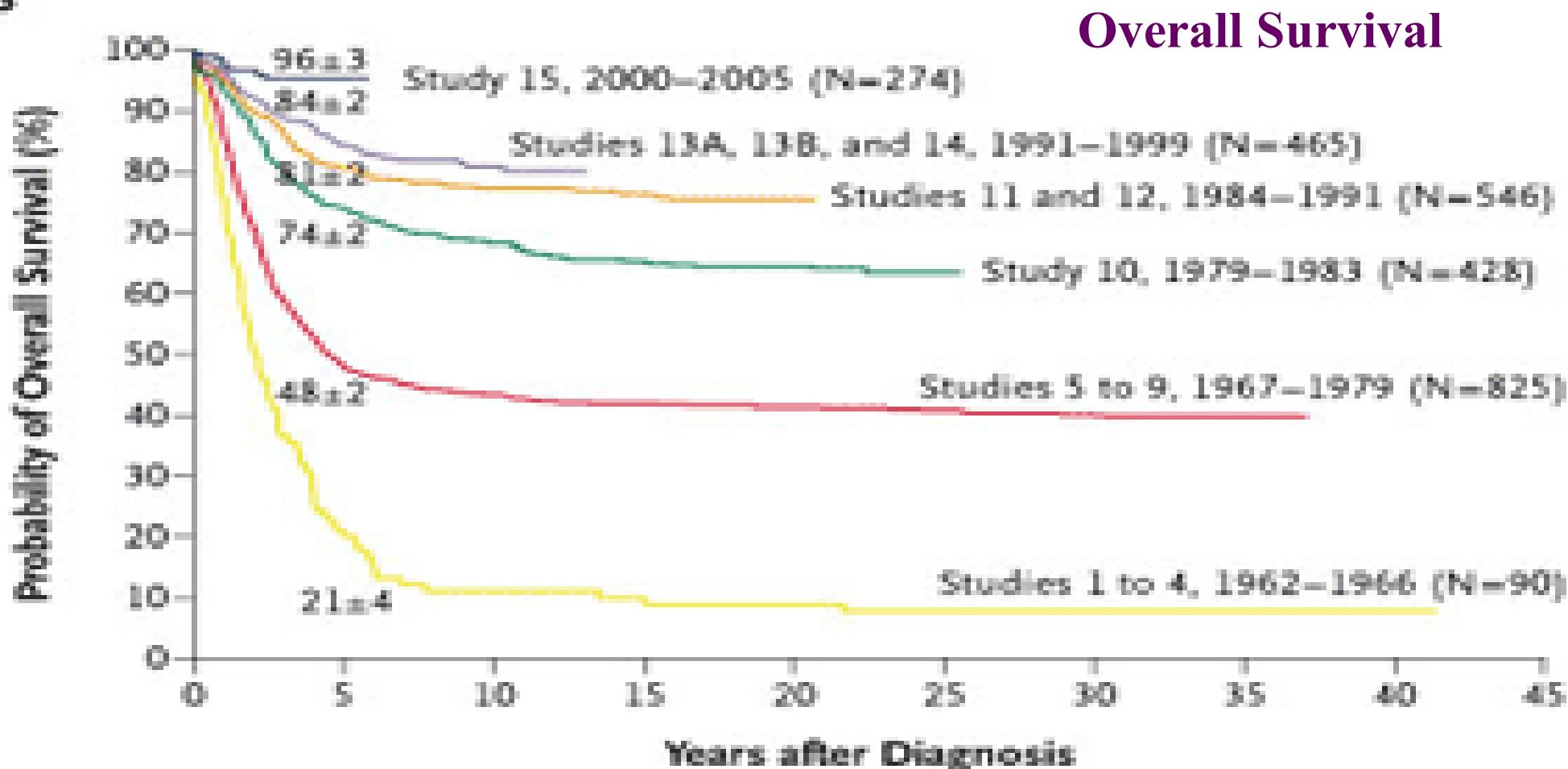
Q.7 Why might, both intrathecal and intravenous systemic chemotherapy be required?



A child with ALL on treatment

Acute Lymphoblastic Leukaemia: treatment results

B





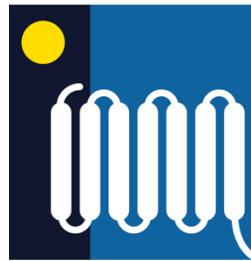
Case 5

- A 45-year-old man presents with abdominal discomfort and swelling
- A Full Blood Count is performed and the patient is urgently referred to the haematology clinic

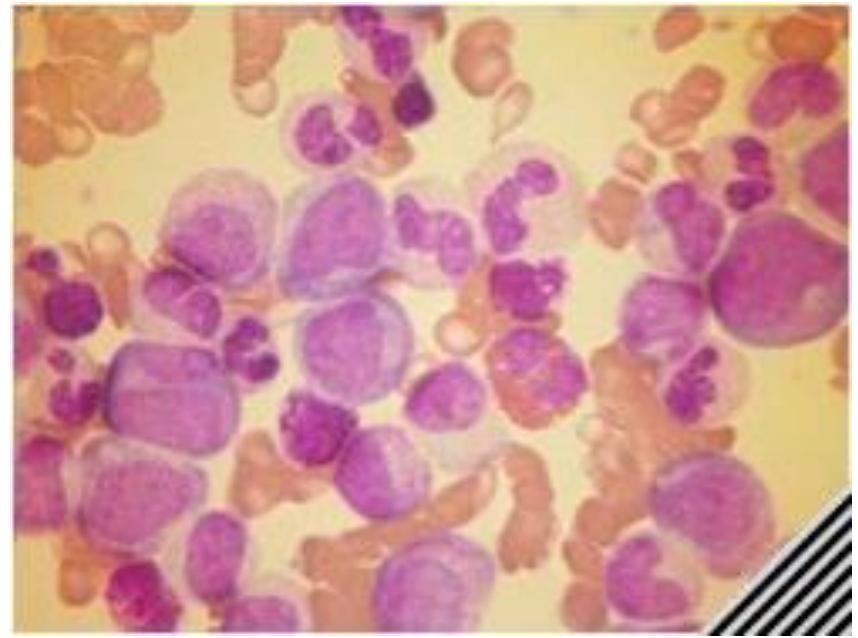
Q.1 What abnormalities are shown on the Full Blood Count?

	Value	Normal Range
Hb (g/l)	135 g/l	133-167
MCV (fl)	87 fl	82-98
White cell count	$117 \times 10^9/l$	4.2 – 11.2
Neutrophils	$110 \times 10^9/l$	0.2 – 7.0
Lymphocytes	$3.2 \times 10^9/l$	1.1 - 3.6
Monocytes	$2.4 \times 10^9/l$	0.3 – 0.9
Basophils	$1.3 \times 10^9/l$	0.0 - 0.5
Eosinophils	$1.0 \times 10^9/l$	0.0 – 0.2
Platelets	$420 \times 10^9/l$	140 - 420

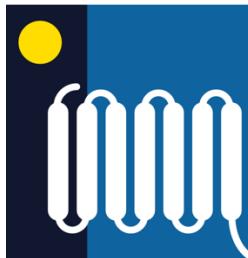
Interpreting white cells on a blood count and film: Case 5



- Is there an abnormality?
- If so, which cell line is abnormal?
- Are there any clues in the clinical history?
- Are there any clues in the blood film?



Q.2 Describe the white blood cell abnormalities shown on the blood film

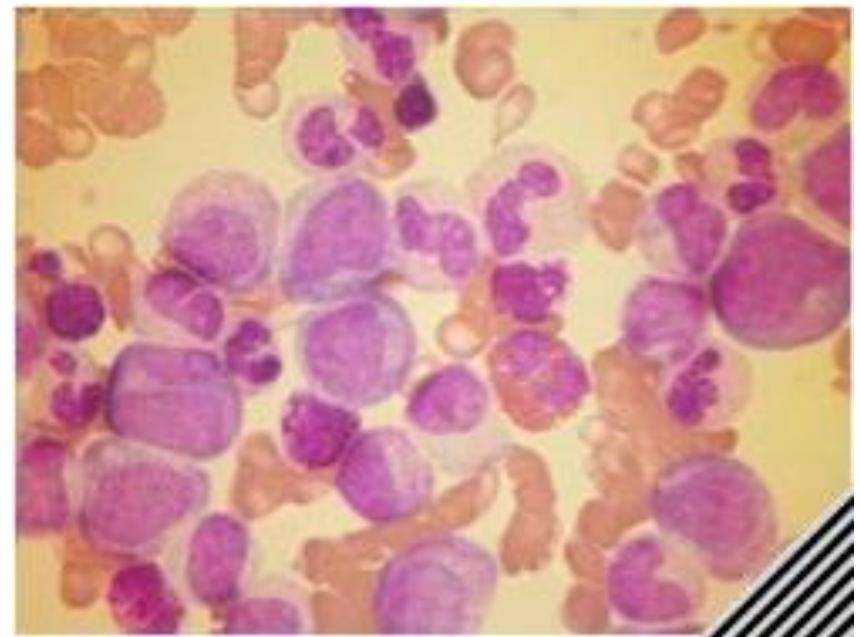


Case 5

- There is an increase in granulocytes — neutrophils, eosinophils and basophils
- The blood film shows an increase in granulocyte precursors — myelocytes and metamyelocytes ('left shift')
- Can you spot the eosinophil?

Q.3 What do you think may be the cause of the patient's abdominal symptoms?

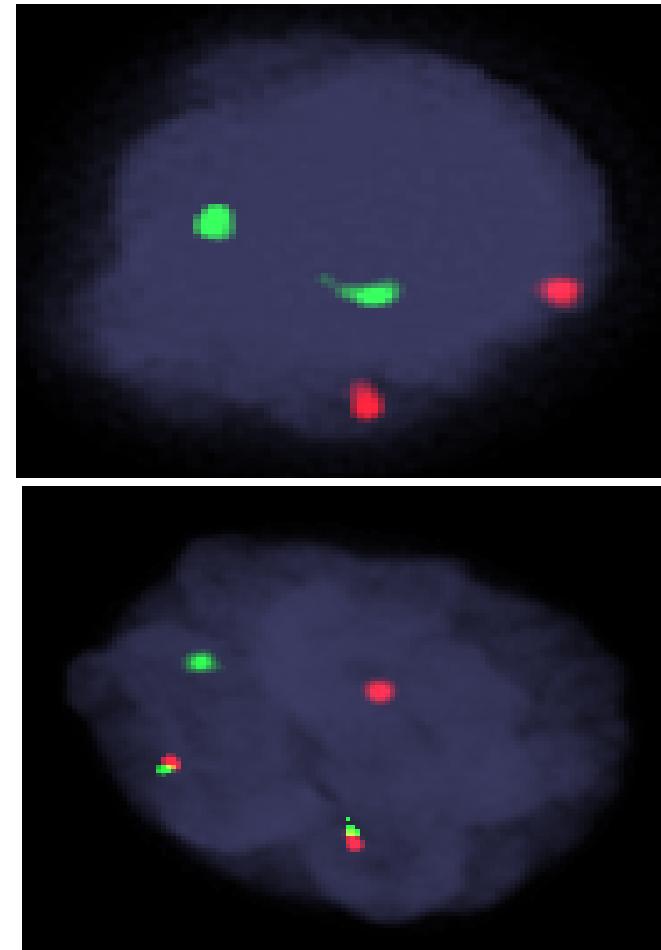
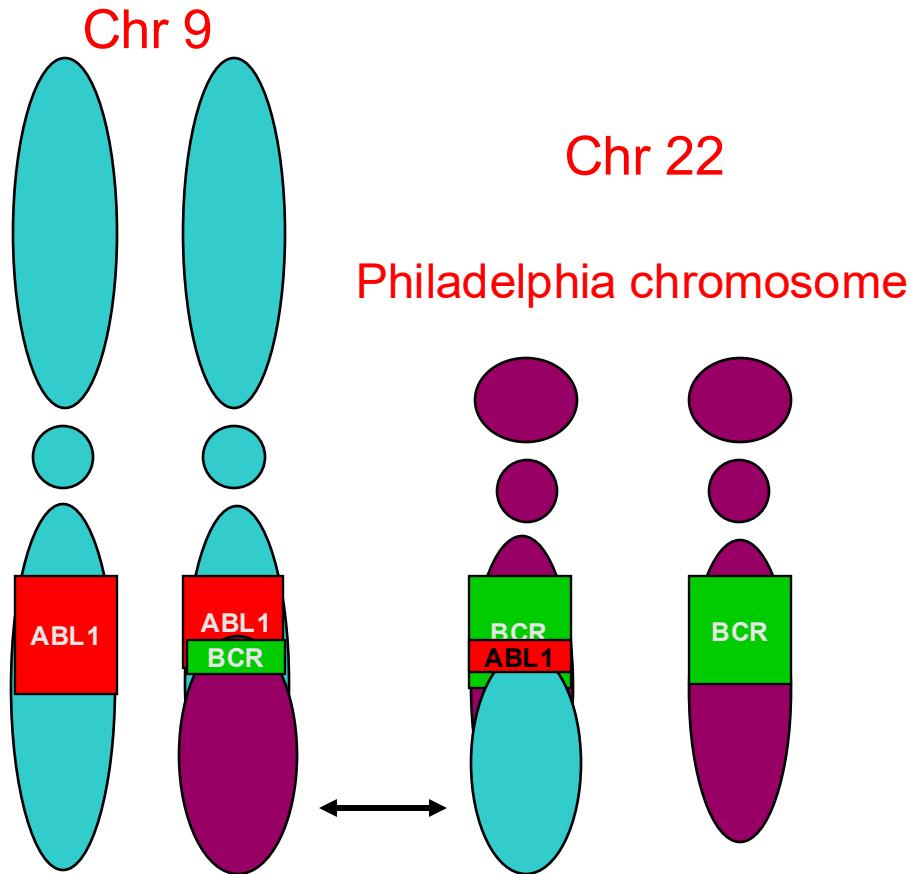
Q.4 A sample is taken for molecular analysis. What abnormality might you expect to find?





Chimeric Gene/ (Dual Colour/Dual Fusion)

ABL1 gene encodes tyrosine kinase enzyme (tightly regulated activity)



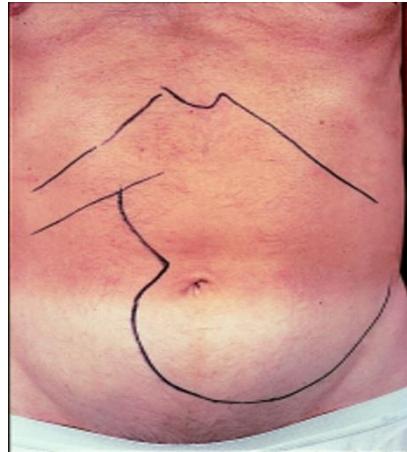
Thanks to Abbott-Vysis

***BCR::ABL1* gene encodes a protein with uncontrolled tyrosine kinase activity, which gives rise to leukaemic clone**

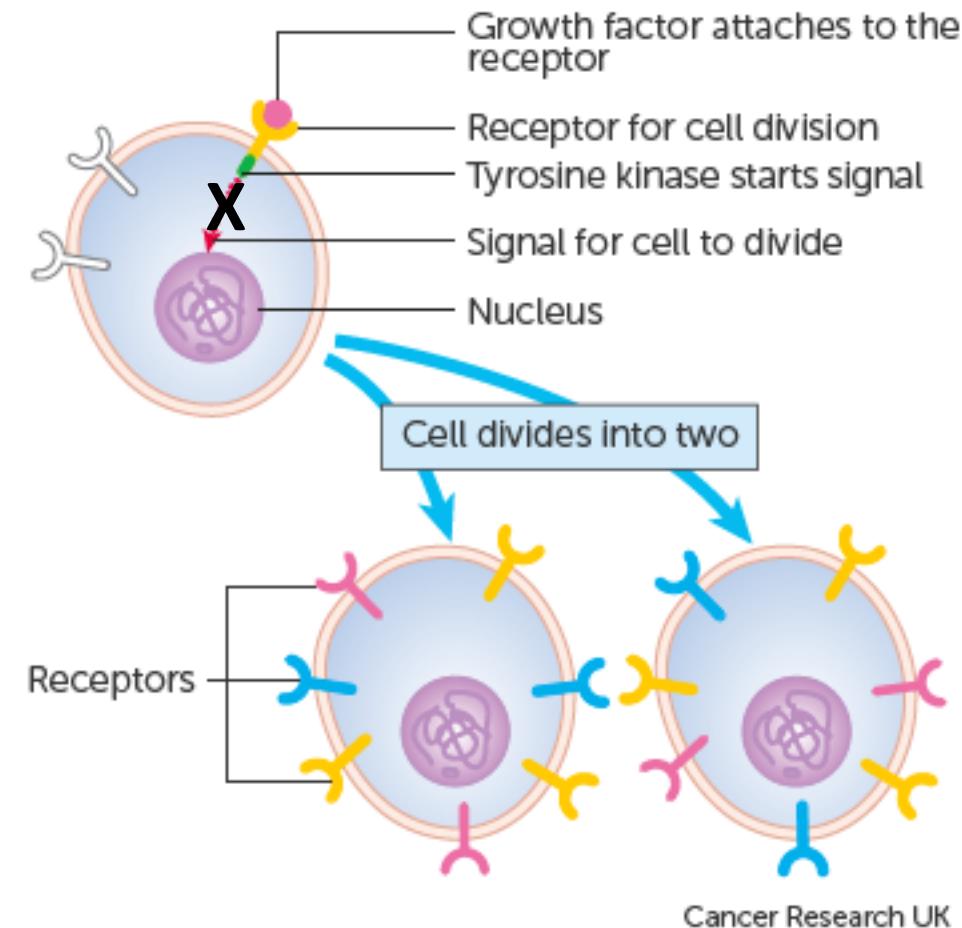


Case 5: Chronic myeloid leukaemia (CML)

- There is an enlarged spleen (splenomegaly)
- The BCR::ABL1 protein signals between the cell surface and the nucleus
- It can be inhibited by specific **tyrosine kinase inhibitors** leading to remission, and potentially cure, of the disease



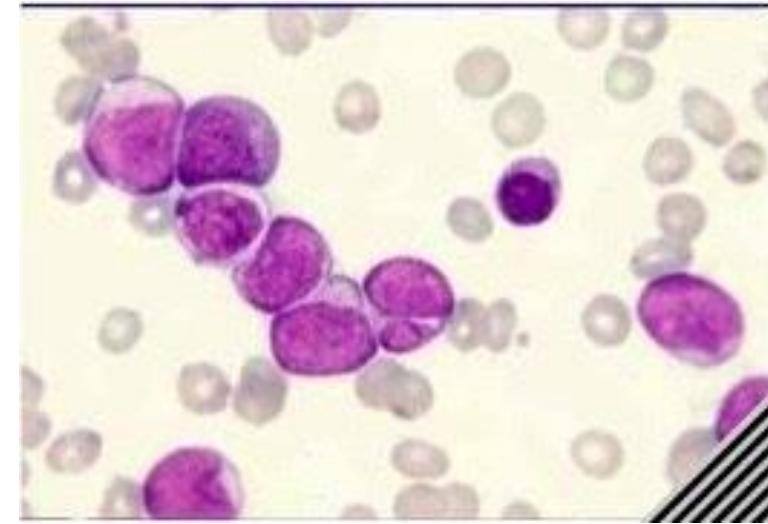
BMJ 1997;314:657



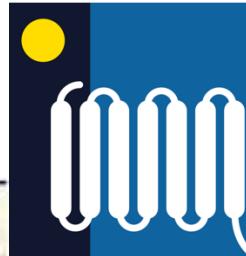
Case 6



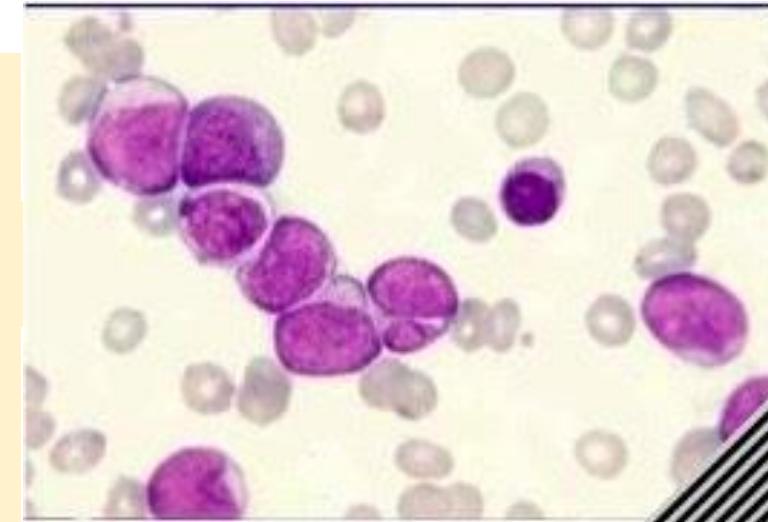
- This blood film is taken from a 60-year old female patient who was referred urgently to the haematology clinic with fatigue, fever, night sweats, weight loss and bony pain
- Describe the abnormalities and likely cause
- How do you account for her symptoms?



Interpreting white cells on a blood count and film: Case 6



- Blast cells with granular cytoplasm (Myeloblasts)
- Anaemia with circulating nucleated RBCs
- Neutropenia
- Thrombocytopenia (low platelet count)



Blast cells can be recognised by:

- large size
- high nucleus/cytoplasmic ratio
- open chromatin pattern of nuclei
- prominent nucleoli
- Note the cytoplasm in these blasts contains granules (unlike Case 4), consistent with myeloblasts, and a diagnosis of Acute Myeloid Leukaemia (AML)
- flow cytometry will characterise these further

What clinical features may be found in leukaemia?

Accumulation of abnormal cells leading to:

- Leukocytosis
- Bone pain (if leukaemia is acute)
- Hepatomegaly
- Splenomegaly
- Lymphadenopathy (if lymphoid)
- Thymic enlargement (if T lymphoid)
- Skin infiltration

Metabolic effects of leukaemic cell proliferation

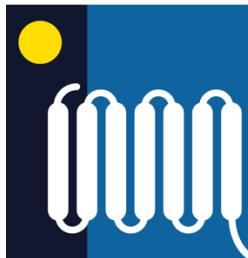
- Hyperuricaemia and renal failure
- Weight loss
- Low grade fever
- Sweating

'Crowding out' of normal haemopoiesis

- Fatigue, lethargy, pallor, breathlessness (caused by anaemia)
- Fever and other features of infection (caused by neutropenia)
- Bruising, petechiae, bleeding (caused by thrombocytopenia)

Loss of normal immune function

- Loss of normal T cell and B cell function
- This is a feature of CLL
(Chronic Lymphocytic Leukaemia)



Session Plan

Part 1 – Discussion of 6 cases

- 6 interactive cases
- The cases are of patients with abnormalities of different types of white blood cell
- They illustrate important principles

Part 2 – Summary

- A 5 - 10 minute discussion at the end will bring it all together

Part 3 – Consolidation

- Post session Reading: Leukaemia - on Insendi
- 'Test yourself' Activity -on Insendi
- **Answers to Tutorial Questions will be available on Insendi at 1700 h on 27th October 2025**

Summary of Cases



Case	Blood count abnormalities	Blood film	Diagnosis
1	Increased neutrophils (neutrophilia), monocytes (monocytosis), eosinophils (eosinophilia)	Neutrophils with toxic granulation	Acute bacterial infection Asthma (likely atopic/allergic)
2	Lymphocytosis	Atypical lymphocytes with basophilic (blue) cytoplasm, scalloped margins and 'hugging' of surrounding red blood cells	Infectious mononucleosis Confirm by testing for heterophile antibodies 'Monospot'
3	Lymphocytosis (incidental finding)	Mature lymphocytes with 'smear' or 'smudge' cells	Chronic Lymphocytic Leukaemia (CLL)
4	Leukocytosis (flagged by analyser), Anaemia, Thrombocytopenia	Lymphoblasts Anaemia, Thrombocytopenia	Acute Lymphoblastic Leukaemia (ALL)
5	Increased neutrophils (neutrophilia), eosinophils (eosinophilia), basophils (basophilia)	Increased granulocyte precursors: myelocytes and metamyelocytes ('left shift')	Chronic Myeloid Leukaemia (CML)
6		Myeloblasts, anaemia, neutropenia, thrombocytopenia	Acute Myeloid Leukaemia (AML)

White cells (leukocytes)

– what abnormalities can occur?



- Changes can be numerical, morphological or both
- **Transient leukocytosis suggest a Reactive (i.e. Secondary) cause** and occurs when a normal or healthy bone marrow responds to an external stimulus such as infection, inflammation or infarction:

bacterial infection:	neutrophilia / monocytosis
viral infection:	lymphocytosis
parasitic infection	eosinophilia
- **Persistent leukocytosis suggests a Primary blood cell disorder-** The leukocyte count is abnormal due to acquired somatic DNA damage affecting a haematopoietic precursor cell giving rise to blood cancers such as leukaemia, lymphoma* or myeloma*

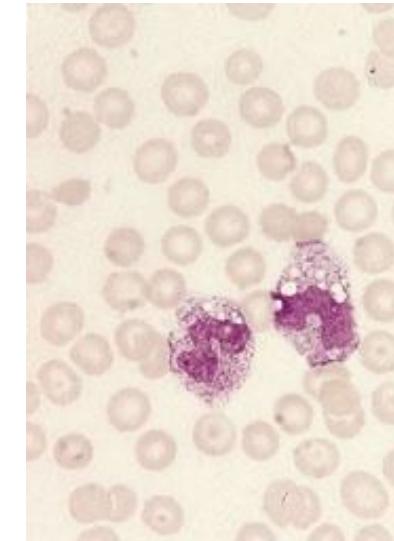
* Taught in late phase curriculum (Y5 Pathology)



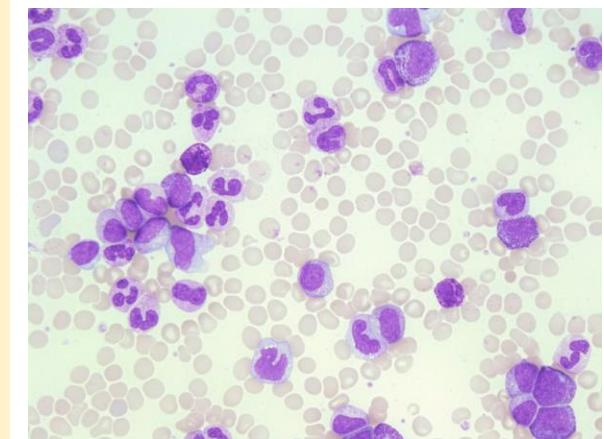
Neutrophilia: too many neutrophils

- Causes: **infection** (particularly bacterial infection), **inflammation**, infarction or other **tissue damage** **Case 1**
- Neutrophilia is also a normal feature in **pregnancy** and may be seen following **exercise** (caused by a rapid shift of neutrophils from the marginated pool to the circulating pool) and after administration of **corticosteroids**
- Neutrophilia may be accompanied by toxic changes and 'left shift' i.e. the presence of early myeloid cells such as metamyelocytes
- **Toxic granulation** is heavy coarse granulation of neutrophils **Case 1**
- **Chronic Myeloid Leukaemia (CML)**, an example of a **myeloproliferative disorder** is a primary blood cancer associated with neutrophilia, basophilia and 'left shift'

Case 5



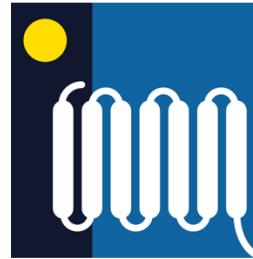
Case 1



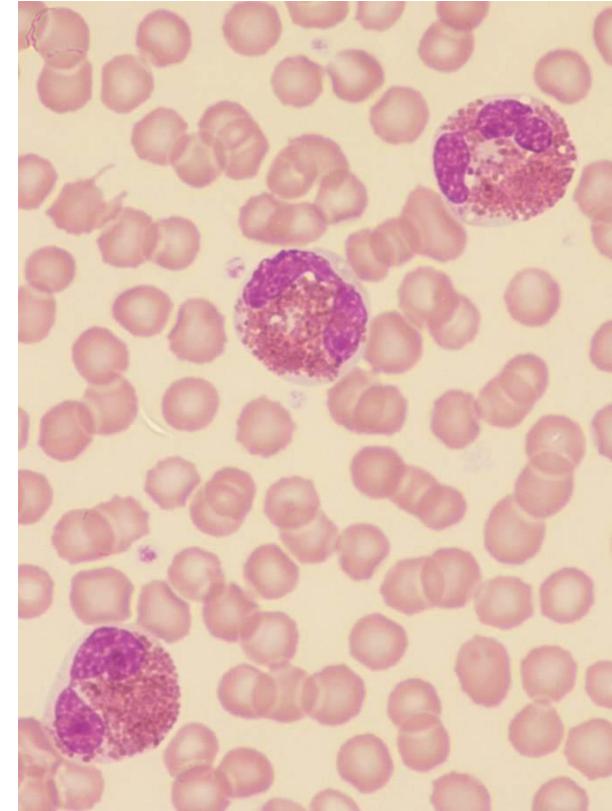
Case 5

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Eosinophilia – too many eosinophils

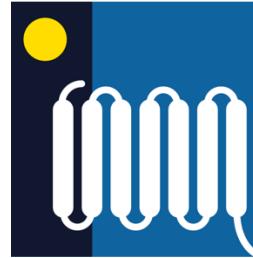


- Usually due to allergy or parasitic infection
 - asthma, eczema, drugs - **Case 1**
- Can occur in some forms of leukaemia e.g. CML
Case 5



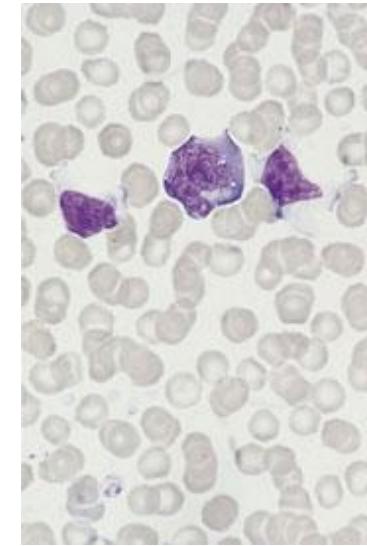
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Lymphocytosis: too many lymphocytes

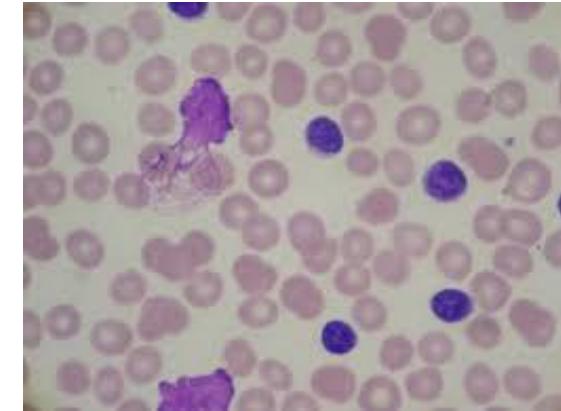


- Often a response to viral infection (**transient**)
- Can result from a lymphoproliferative disorder
e.g. chronic lymphocytic leukaemia (**persistent**)

Case 2



Case 3

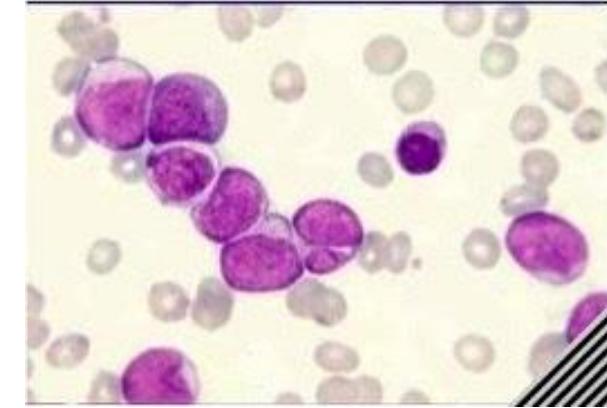


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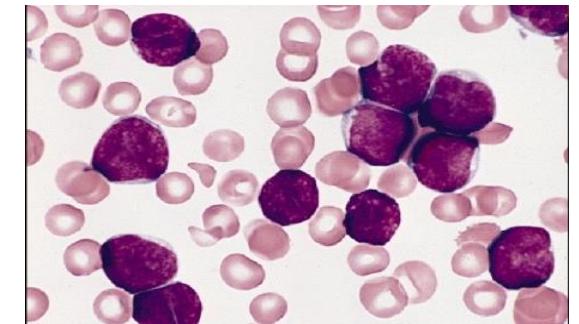
What is the difference between acute and chronic leukaemias?



- In **Acute** Leukaemia (**AML** or **ALL**) there is an increase in very immature cells (**myeloblasts or lymphoblasts**) with a failure of these to develop into mature leukocytes
- In **Acute** leukaemia, the bone marrow is infiltrated by immature blast cells, resulting in impaired haemopoiesis: **blast cells** also circulate in the peripheral blood and can be seen on the blood film
- If **Acute** leukaemias are not treated, the disease is very aggressive and patients die quickly

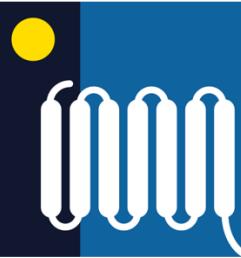


Case 6

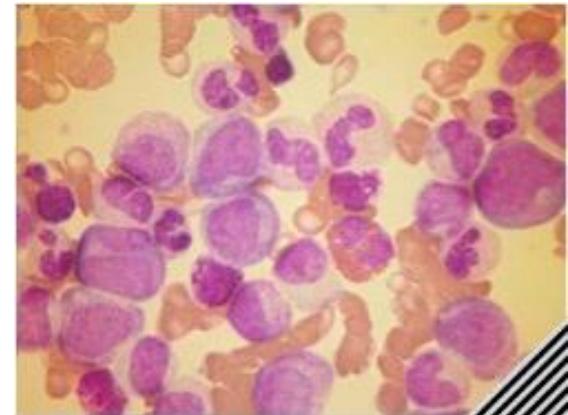
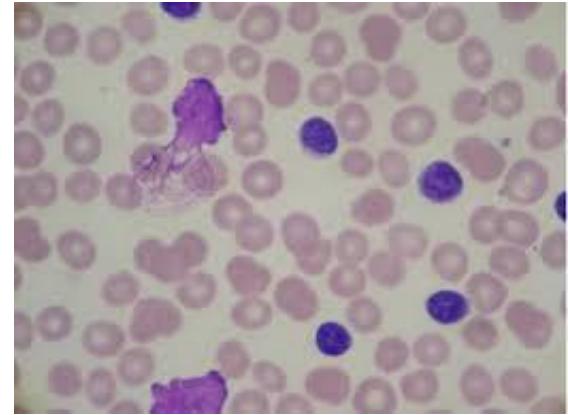


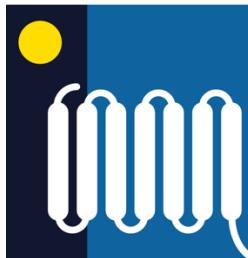
Case 4

What is the difference between acute and chronic leukaemias?



- In **Chronic** Leukaemias the leukaemic cells are mature, although abnormal: granulocytes (**CML, Case 5**) or lymphocytes (**CLL, Case 3**)
- In **Chronic** Leukaemias the disease and deterioration go on for a long period of time
- In **CML**, the mature end cells are still able to function; in **CLL** the lymphocytes are functionally useless and there is a loss of normal immune function





Session Plan

Part 1 – Discussion of 6 cases

- 6 interactive cases
- The cases are of patients with abnormalities of different types of white blood cell
- They illustrate important principles

Part 2 – Summary

- A 5 -10 minute discussion at the end will bring it all together

Part 3 – Consolidation

- Post session Reading: Leukaemia - on Insendi
- ‘Test yourself’ Activity - on Insendi
- **Answers to Tutorial Questions will be available on Insendi at 1500 h on 27th October 2025**