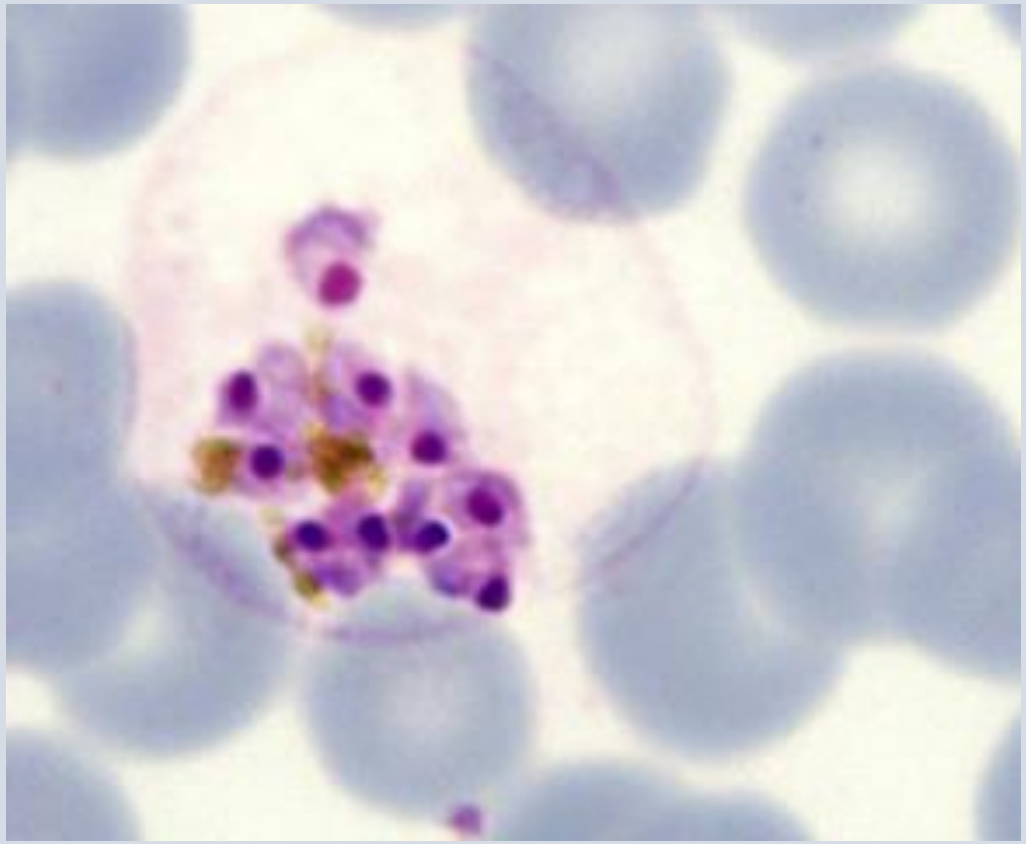
Morphology, mistakes and AI

John Burthem

A (very) short review of morphology



Beauty,
Simplicity,
Education,

Longevity,
Transmissibility,
Add value to image

Components

1. How do humans perceive images?
2. How do “human errors” arise?
3. How best to help avoid these errors?
4. Some personal reflections on AI/machine learning in morphology

1. HOW DO HUMANS PERCEIVE IMAGES?

How do you “see” an image?

(are you better than a machine)

You have 20 seconds to look at this image. **What do you see?**

You used heuristics

- Evolutionary mechanism
- Allow us rapidly to identify specific features or pattens with useful accuracy
- Eye is drawn to any unexpected or unusual elements or possible threats
- We then rapidly evaluate, classify and act, often using very small clues
- Particularly useful in *stressful* situations: rapidly identify potential threats

What you (probably) did

Emotional overlay

Processing boundaries and impose shape detail

Ignored the “familiar” and prioritised unexpected items

- Classification
- Prioritisation
- Reinforcement
- Interpretation
- Completion of task

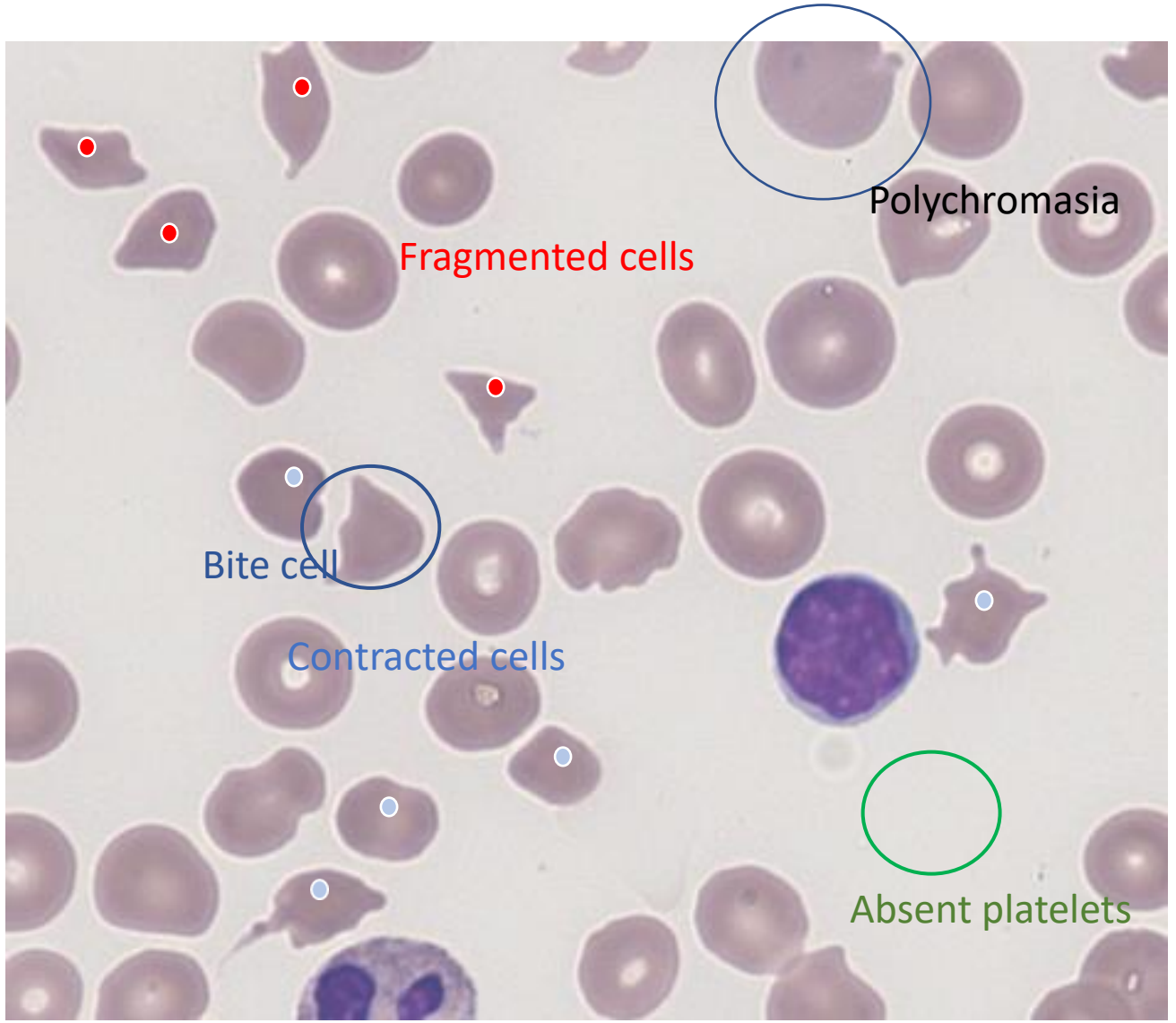
Blood film analysis employs very similar processes

(Emotional overlay)

Processing boundaries and impose shape detail

Ignored the “familiar” and prioritised unexpected items

- Classification
- Prioritisation
- Reinforcement
- Interpretation
- Completion of task



Likely MAHA

SEEK OTHER EVIDENCE, TELEPHONE RESULT

However, heuristics may not aways be helpful

These rapid decision processes that enable rapid and effective interpretation of complex images can also be a source of error:

We apply personal rules that allow what we see to be put together, these rules can lead to **BIAS**

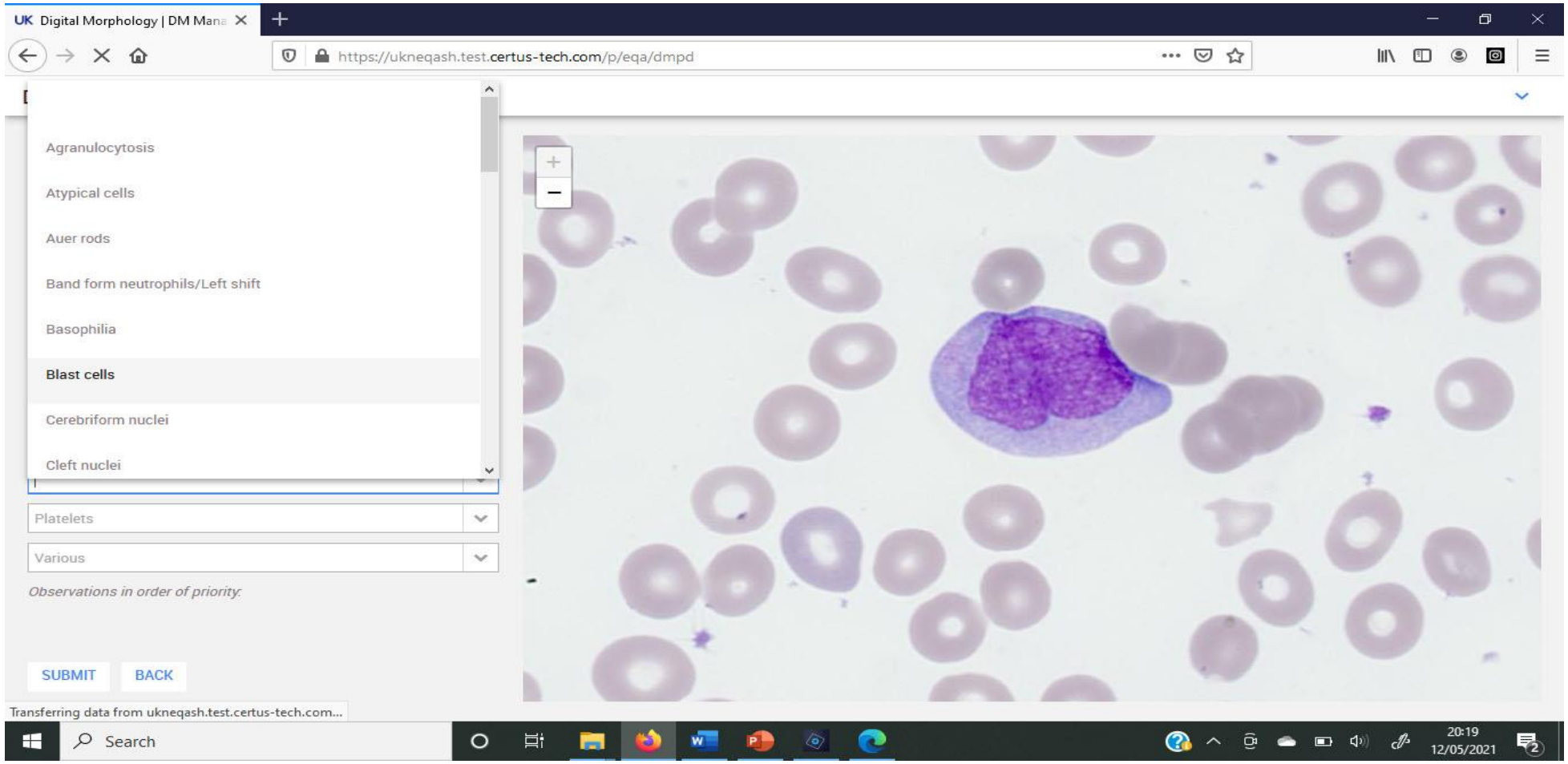
The UK NEQAS(H) digital morphology scheme provides a resource to look at this:

- 18 years, 6 cases per year, each case is completed by 1000-1500 users with a range of skills
- All participants look at an identical digital slide
- We collect anonymised data of responses:

UK NEQAS (H) Digital CPD scheme

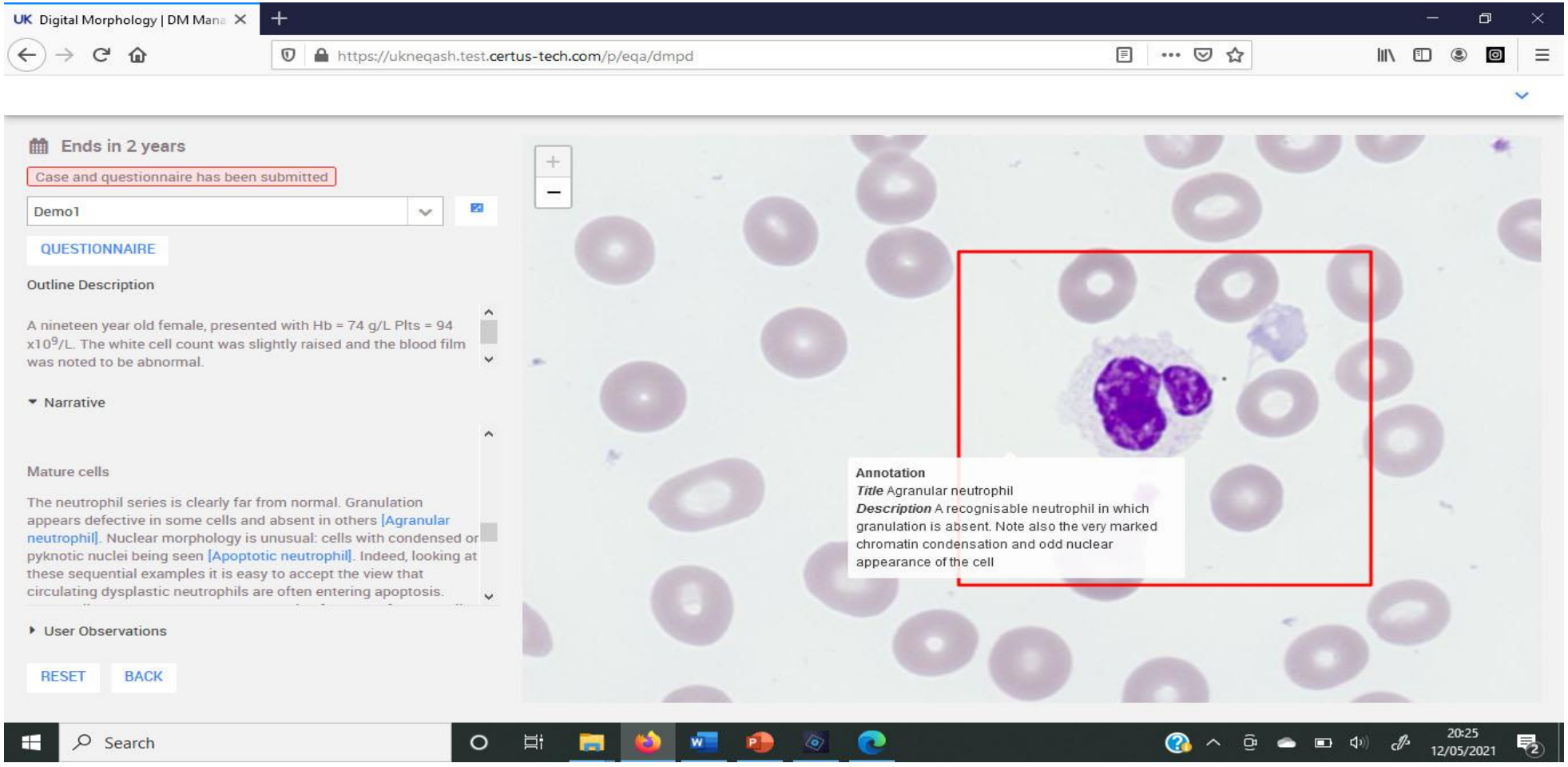
Entries for:
Features (coded)
Decisions (coded)

Entry for:
Diagnosis (text)***



UK NEQAS (H) Digital CPD scheme

Your reward:
Annotation
CPD
Skills comparison
Retain slide



Our reward: the data we receive

Diagnosis (free text)

Coded action

Coded features

(average n=1500)

Diagnosis	Action	Ist	2nd	3rd	4th	5th	
leukamia	E	102	137	203	106	0	
lymphoma	E	104	108	119	127	0	
leukamia	B	104	132	128	109	115	
leukamia	B	106	127	114	124	102	
leukamia	B	106	132	122	311	321	
leukamia	B	106	132	203	126	305	
leukamia	C	106	123	134	208	104	
leukamia	B	106	102	308	0	0	
leukamia	B	106	102	133	127	0	
leukamia	B	106	114	132	127	101	
lymphoma	A	107	115	108	135	203	
lymphoma	B	107	135	205	0	0	
lymphoma	E	107	108	205	204	320	
lymphoma	E	108	122	205	208	123	

Some people identify features incorrectly or make incorrect interpretations!

This is CPD!

However, in real life this may have a big impact

- we felt that we had a resource to look at why!

2. UNDERSTANDING “HUMAN ERROR” (IN MORPHOLOGY)

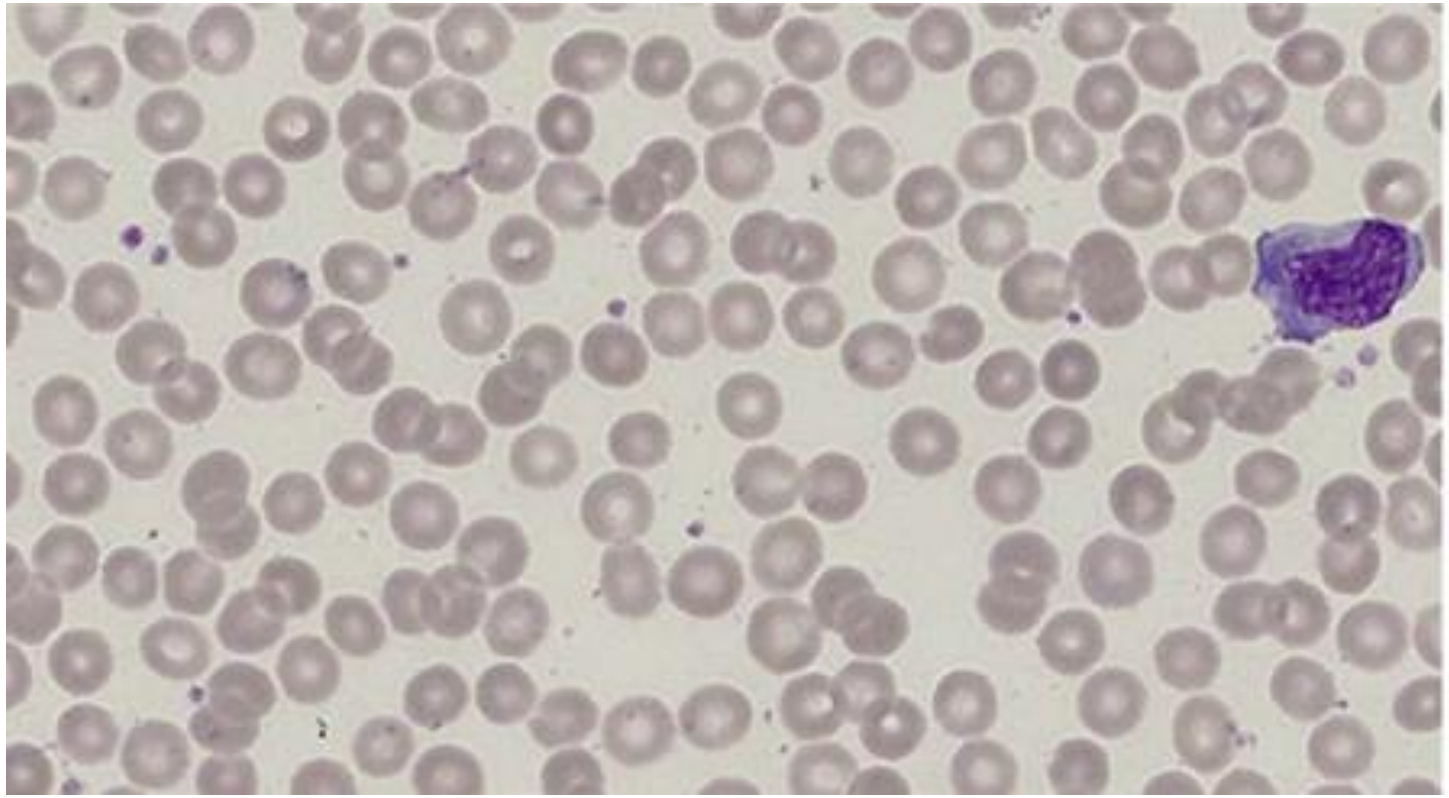
Using our data we identified two (partly) distinct mechanisms of error in our participants:

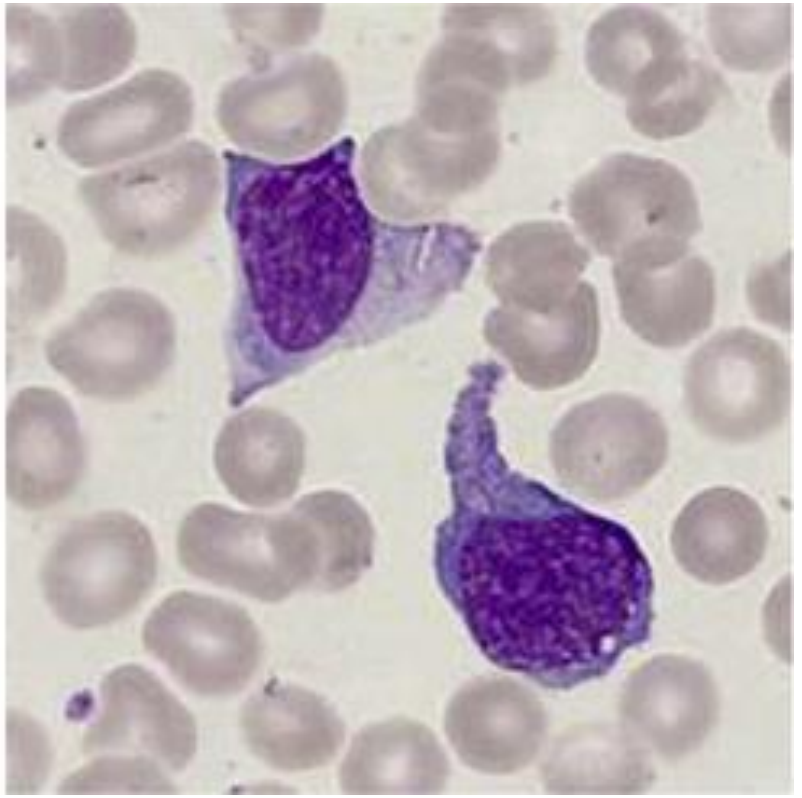
A. “KNOWLEDGE ERRORS”: misidentification, failure of interpretation

B. “HEURISTIC ERRORS”: heuristic biases relating to how we view images

** Remember our participants have a range of skills and responsibilities*

A. Knowledge errors:





Viral infection (EBV)

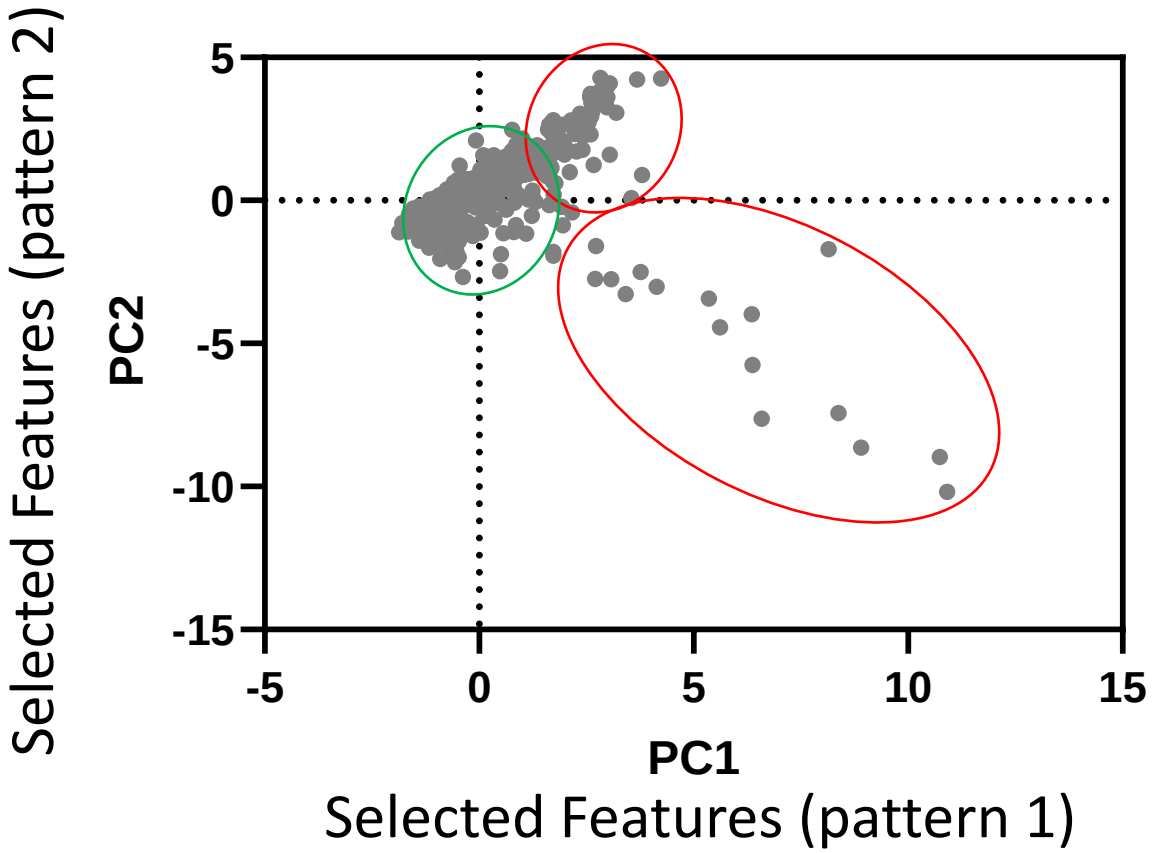
Results: Viral 421; lymphoma/leukaemia 138

A. Knowledge errors (2): possible error sources

- Failure to find the abnormal cells?
- Failure to classify the cells correctly?
- Failure to correctly prioritise or interpret the findings?
- (emotional overlay – the negative consequence of a missed serious diagnosis)

Knowledge error (3)

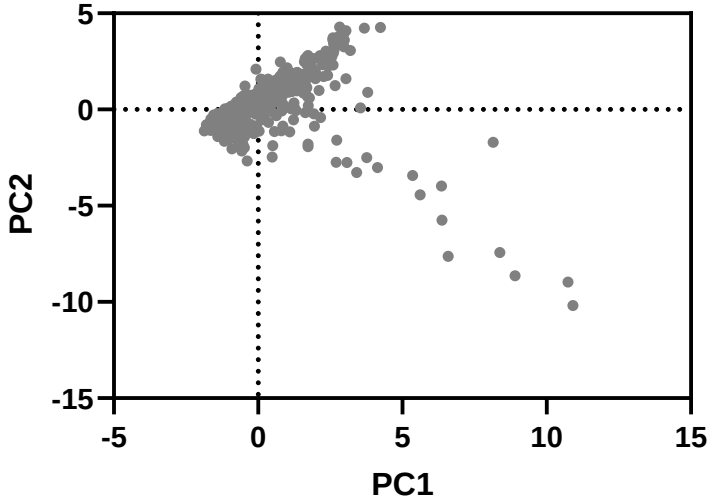
PCA - Comparison of features selected and diagnosis made: this allows us to identify patterns of error

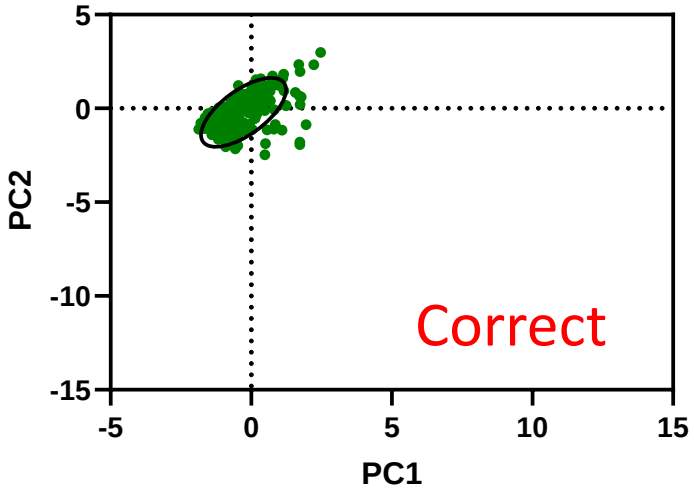


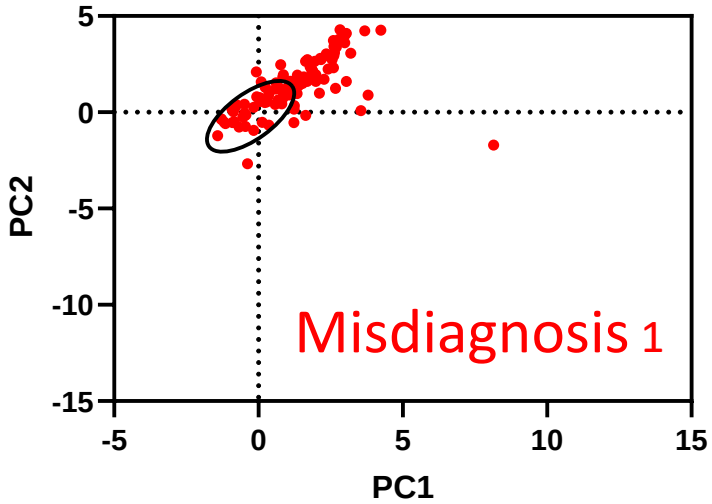
What is the significace of the outliers?

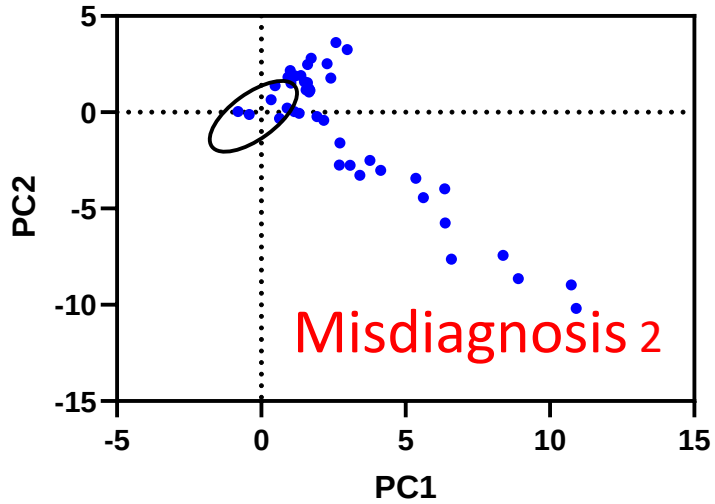
Knowledge error (3)

PCA and Random Forest - Comparison of features selected and diagnosis made: this allows us to identify patterns of error





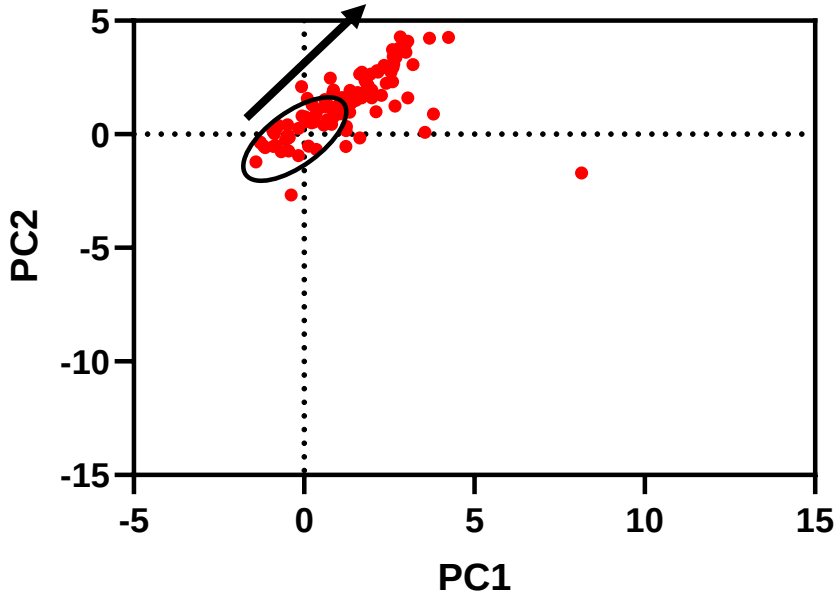


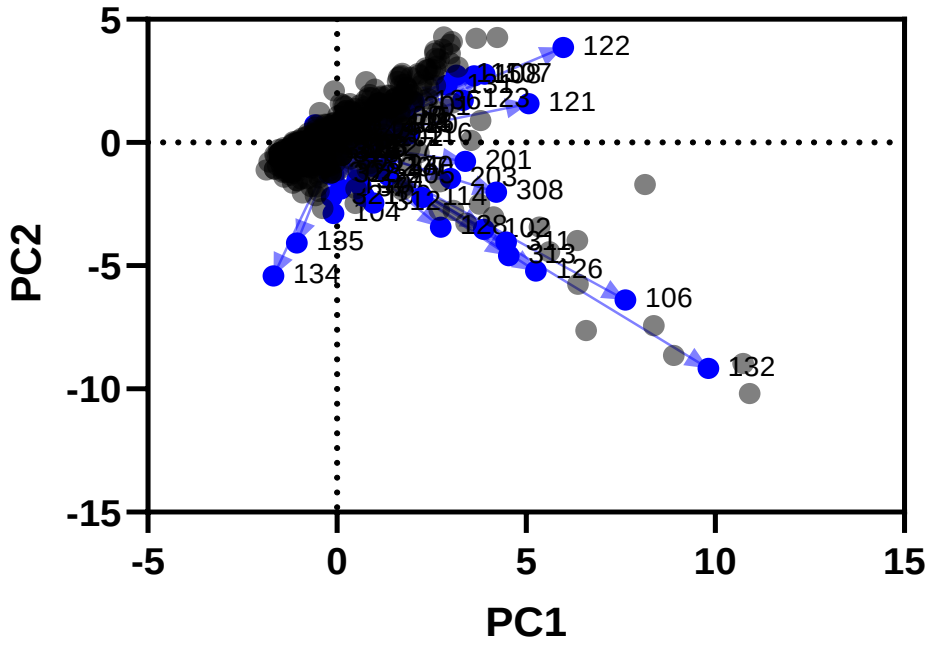


Knowledge error (4)

Error pattern 1

People diagnosing **NEOPLASTIC LYMPHOID CELLS**





122 Lymphocytosis neoplastic appearance

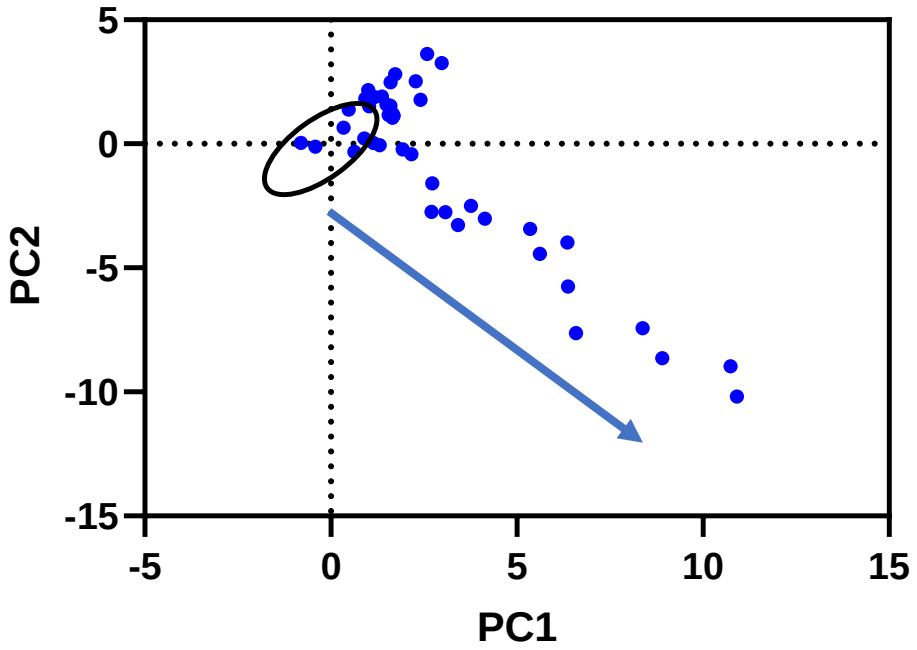
121 Lymphoblasts

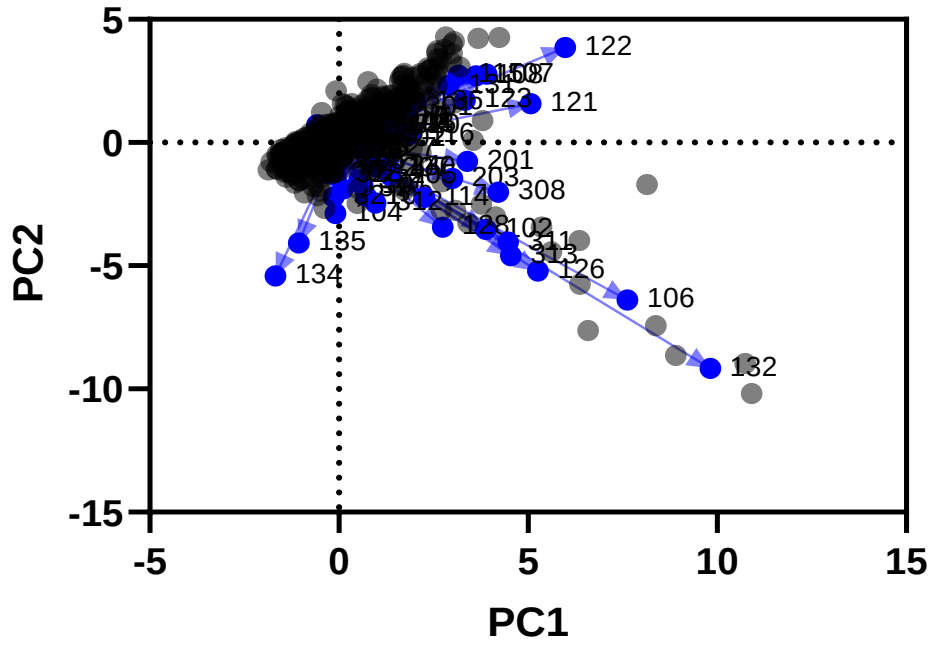
107 Cerebriform nuclei

Knowledge error (4)

Error pattern 2

People diagnosing ACUTE LEUKAEMIA CELLS





132 Promyelocytes

106 Blast cells

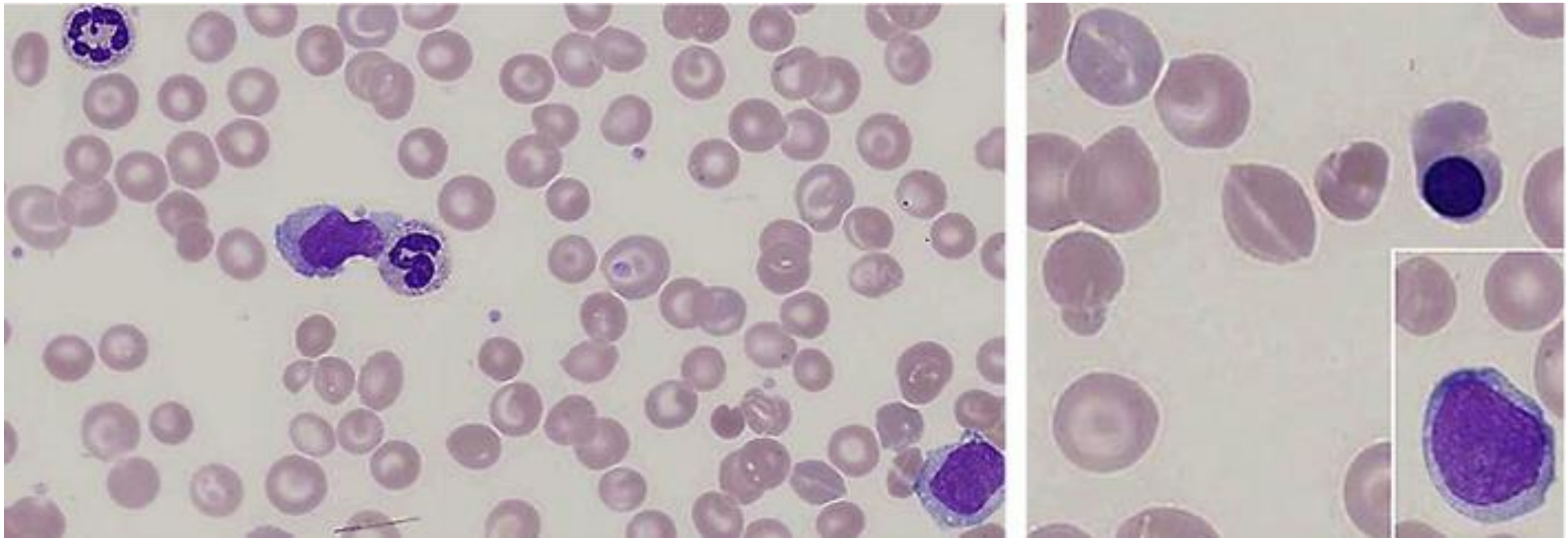
126 myelocytes

Conclude

- For cases with “low complexity” i.e. recognising predominantly a single morphological entity the predominant errors are of “knowledge”
- i.e. mistakes of feature identification or feature interpretation

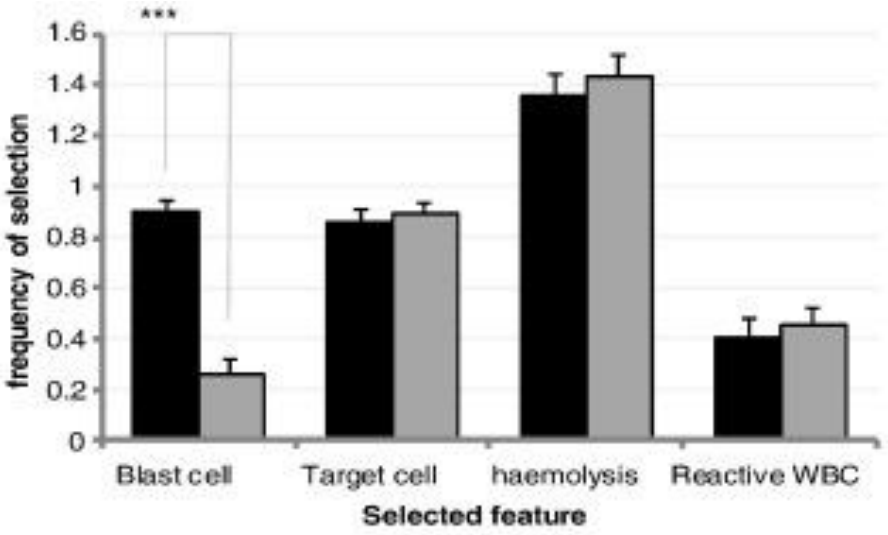
- Could we improve outcomes through access to knowledge?

A. Heuristic errors (bias)



Haemoglobin C disease (HbCC) and acute myeloid leukaemia

Heuristic errors (biases) 1



Most features selected were remarkably similar for those diagnosing AML or those diagnosing a non-malignant condition!

Those diagnosing AML were more likely to **see or report** blast cells.

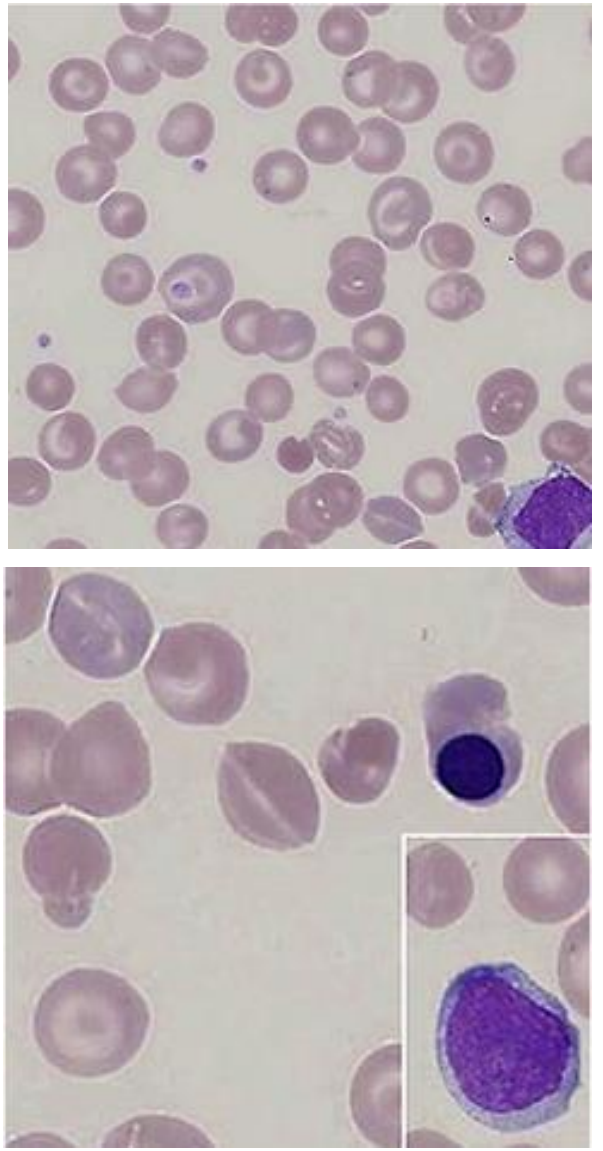
A. Heuristic errors (bias) – this is not simply a knowledge error

- We know from experience that UK NEQAS participants identify HbCC or HbSC well – 65%
- We also know that identification of acute leukaemia is excellent – 80-90%
- Yet when presented together the identification rate was different:
    - Only just over half diagnosed AML
    - Others diagnosed: Haemolysis, liver disease, reactive conditions
    - Only 10% were fully correct

i.e. complex morphology creates unexpected errors

Heuristic errors (biases) 2

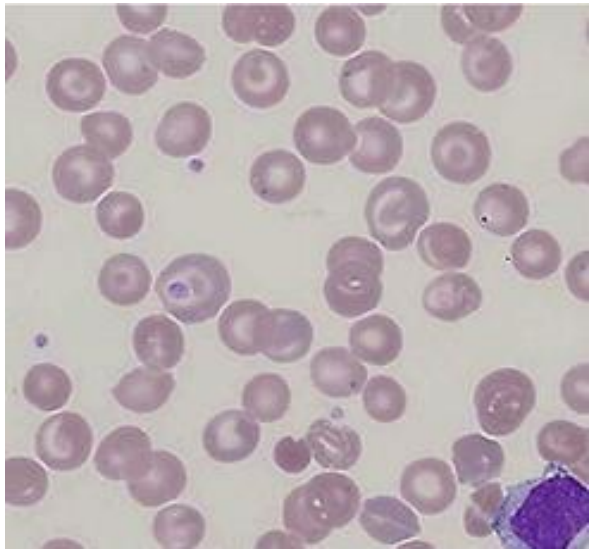
The error mechanisms of people looking a complex problems are fairly well established in many contexts e.g. radiology

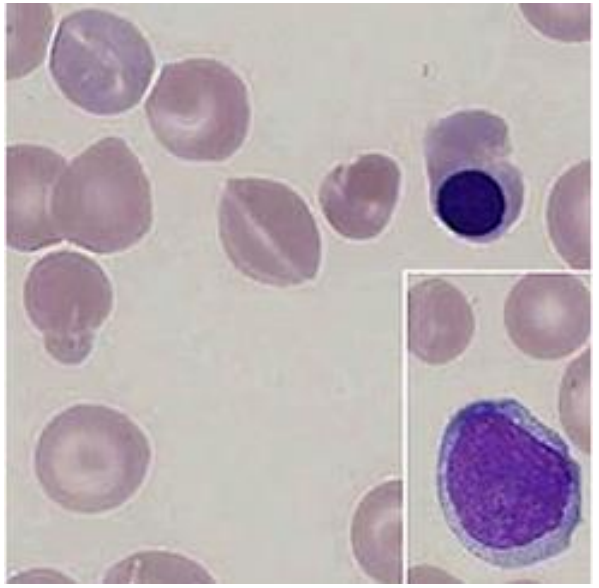


Brereton, M., et al. (2015). Do We Know Why We Make Errors in Morphological Diagnosis? EBioMedicine, 2(9), 1224–1234

Heuristic errors (biases) 2

Biases of imaginability:
Too much to think about
Inattention error
Simplification bias: inappropriately assigning features as a single related group

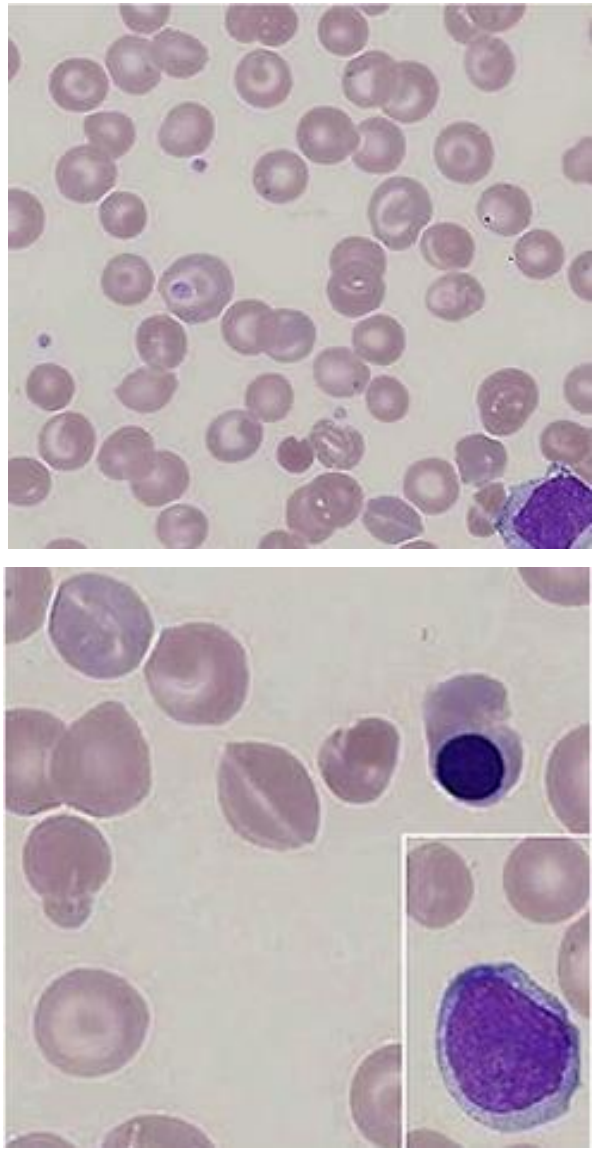




Heuristic errors (biases) 2

Anchoring bias:

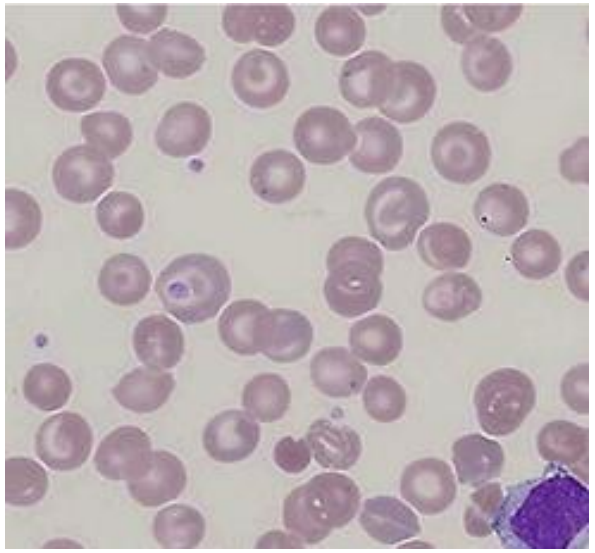
Prematurely fixing on one aspect (satisfaction of search) then ignoring other findings

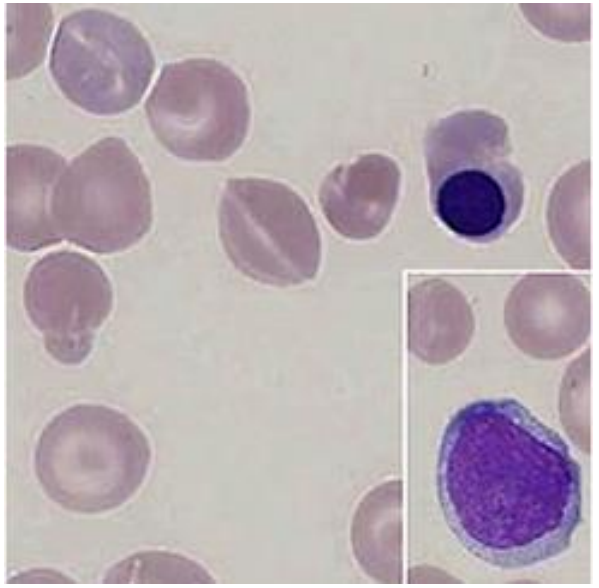


Heuristic errors (biases) 3

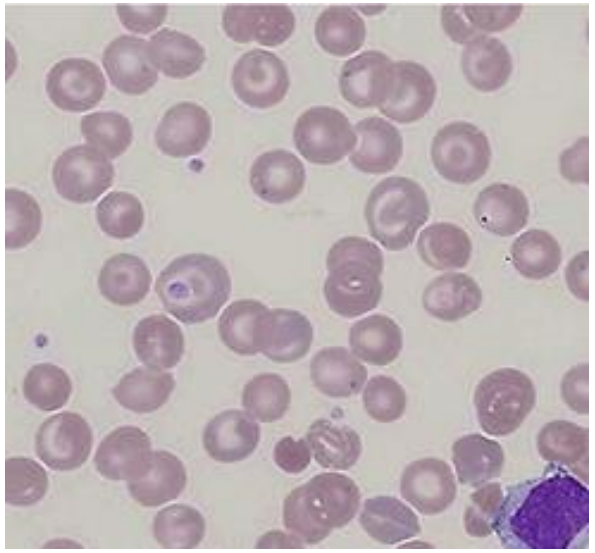
Reinforcement biases:

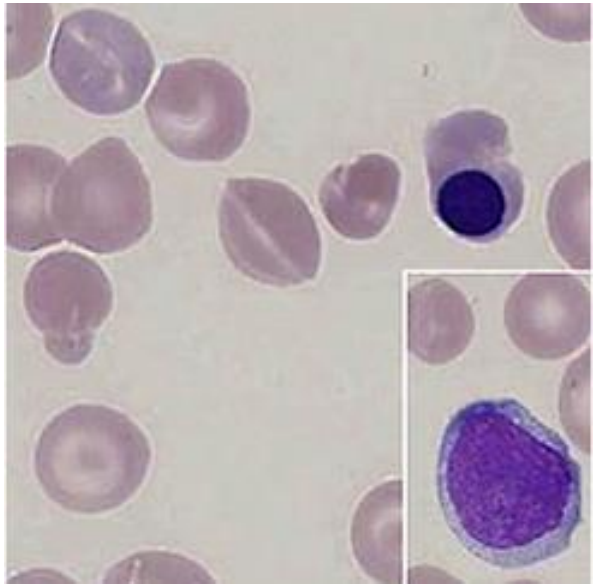
Associative thinking – trying to make the features fit the preferred diagnosis





Heuristic errors (biases) 3





Overlay:
Emotional response
Pressure to complete

Premature completion of task

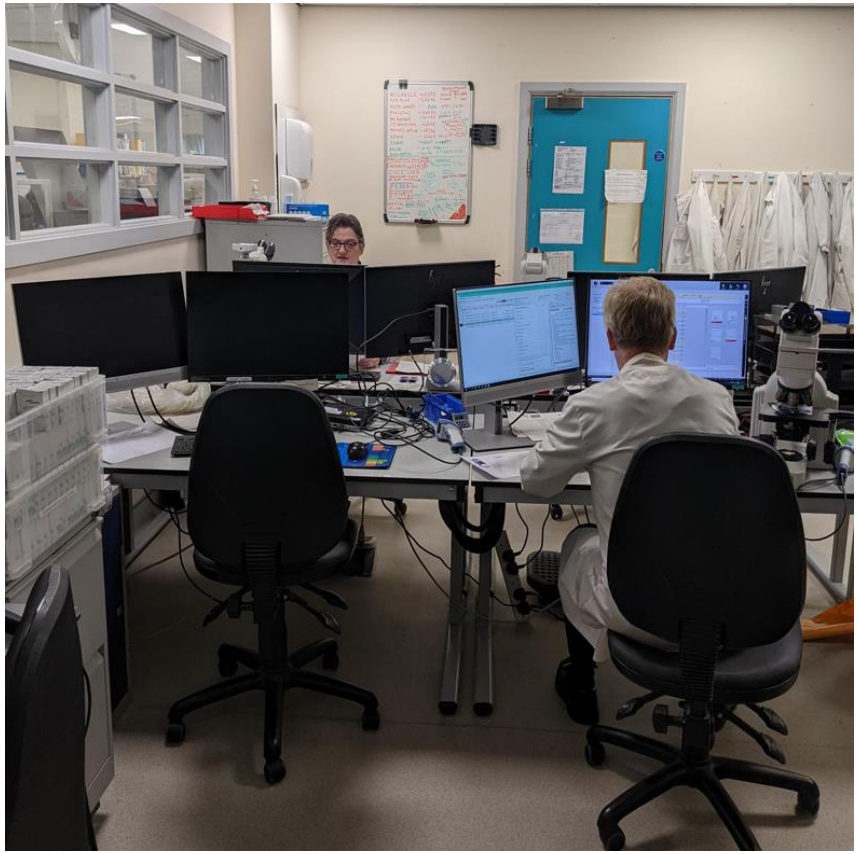
Conclude

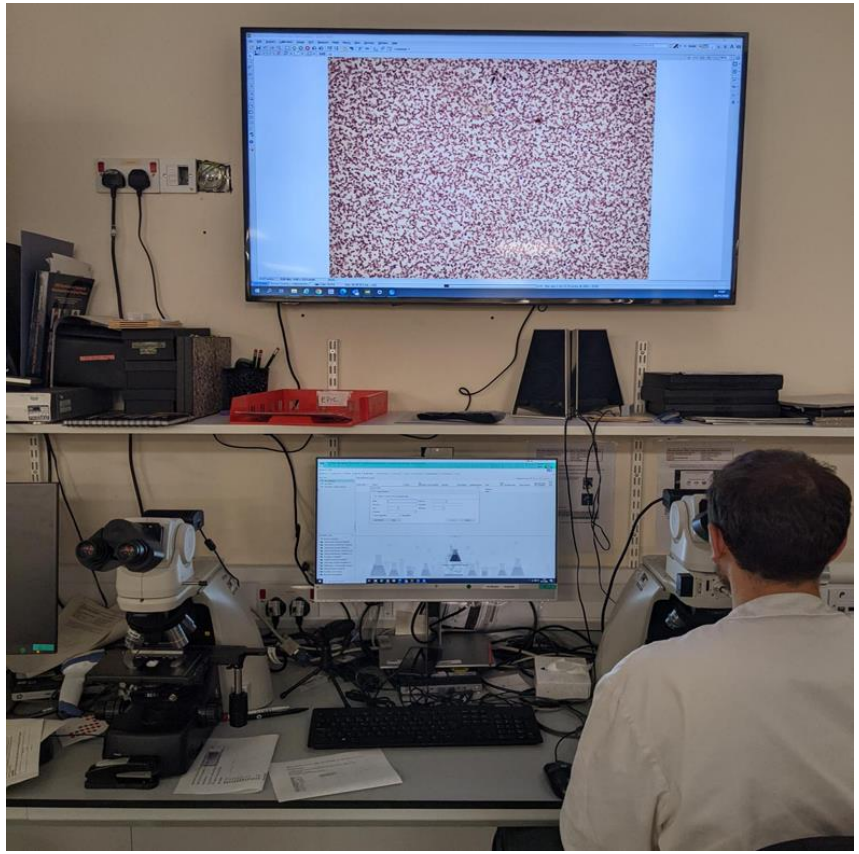
- For cases with higher complexity the predominant errors are of “heuristic”

3. **REDUCING KNOWLEDGE ERRORS**

Hutchinson, C., et al. (2021). The Use and Effectiveness of an Online Diagnostic Support System for Blood Film Interpretation*Journal of medical Internet research*, *23*(8), e20815. https://doi.org/10.2196/20815

In the lab we ar now surrounded by technology ….

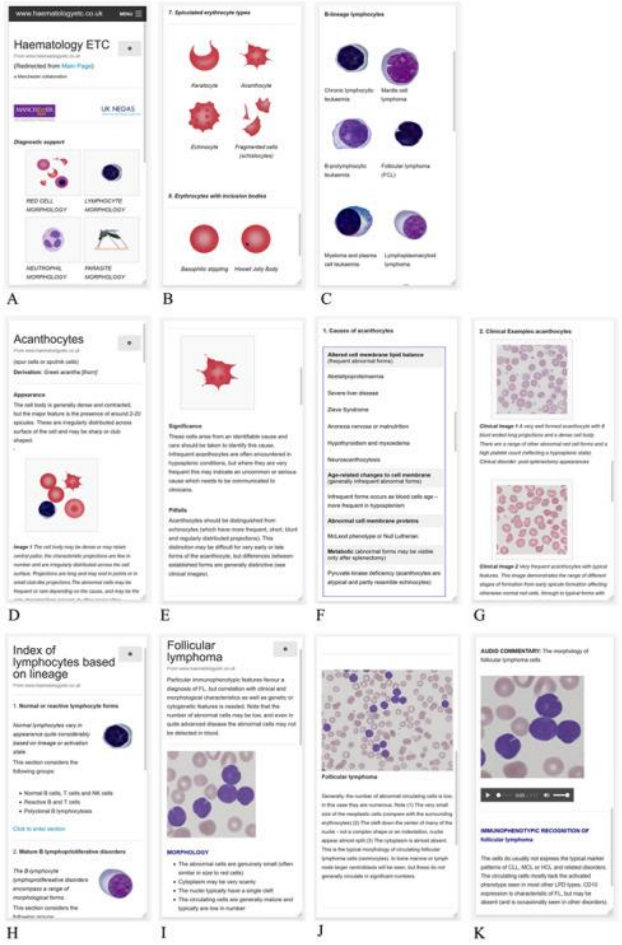




Would added information help?

In particular if that information was provided digitally

Connected information!!!!! (*www.haematologyetc.com*)



Testing interventions re-use of cases

- Selected cases used earlier were re-released (>8 years old) – we can do this!
- Participants were given voluntary access to digital help
- We were able to directly compare results of our two separate surveys

Was it used?

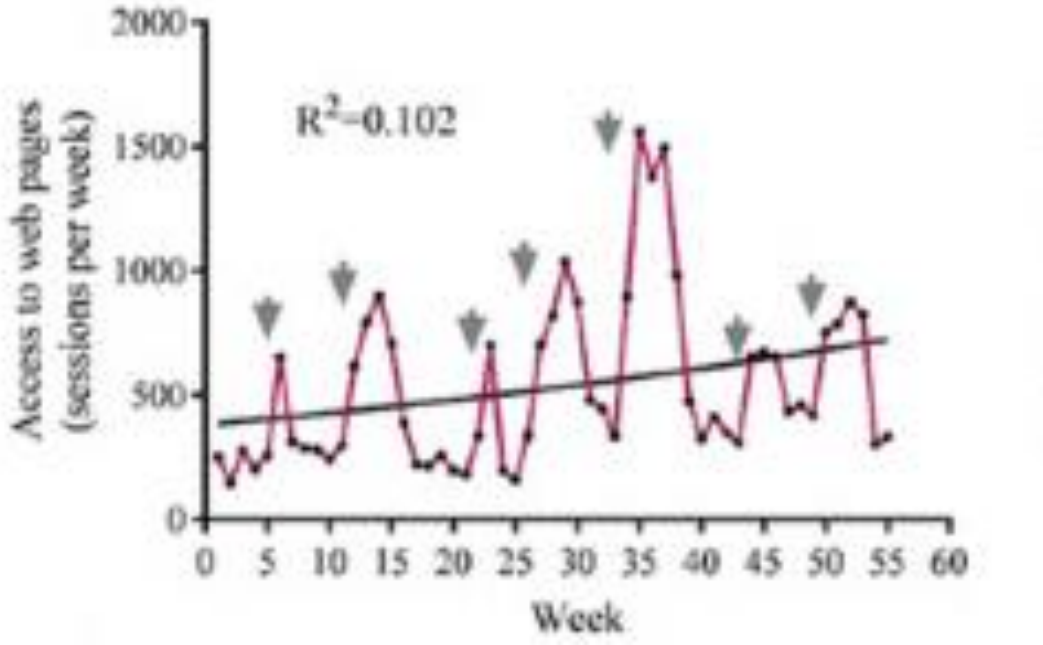
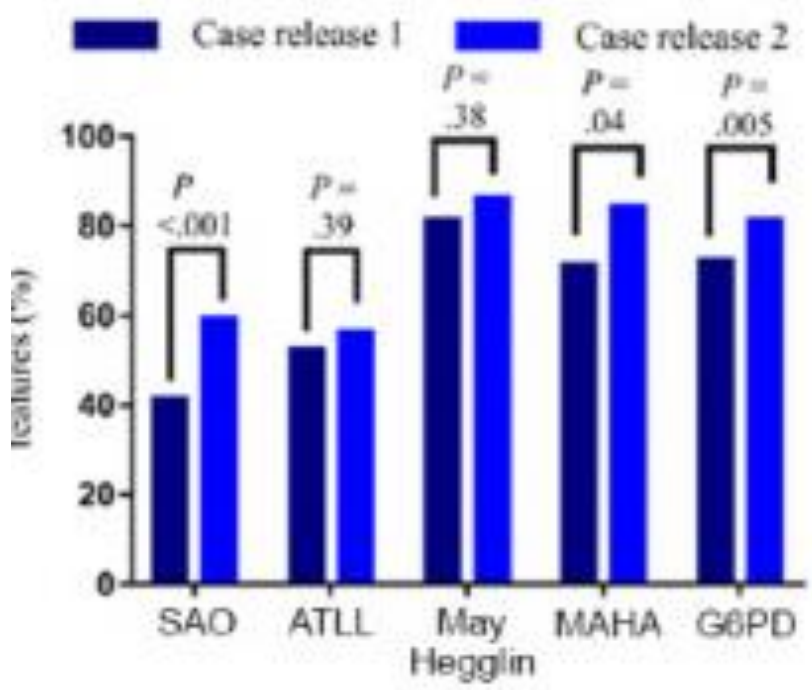
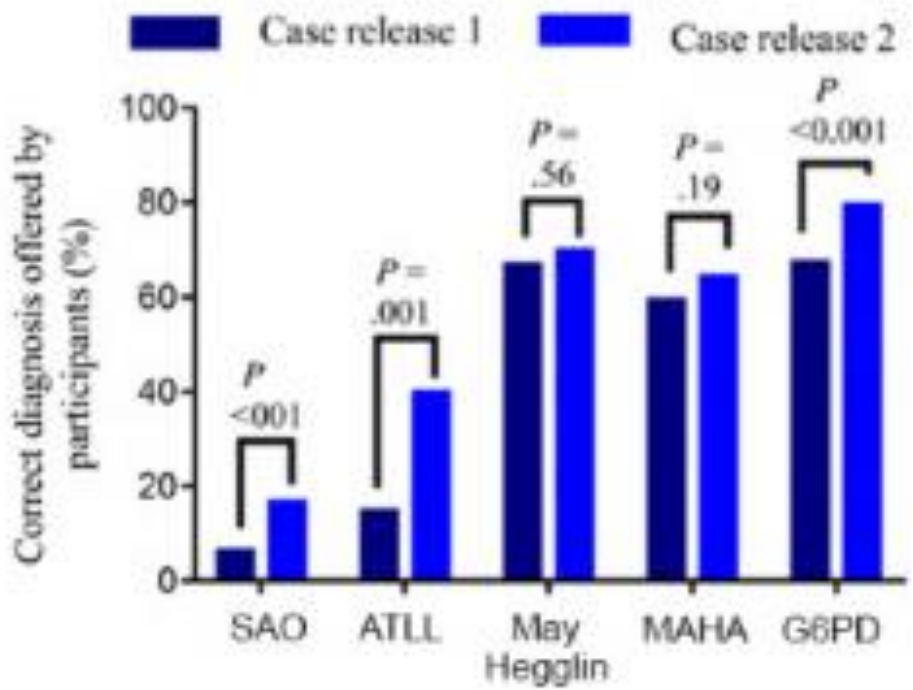


Image viewing of the appropriate web pages was high (and selective)

Did it help?



Feature selection was improved



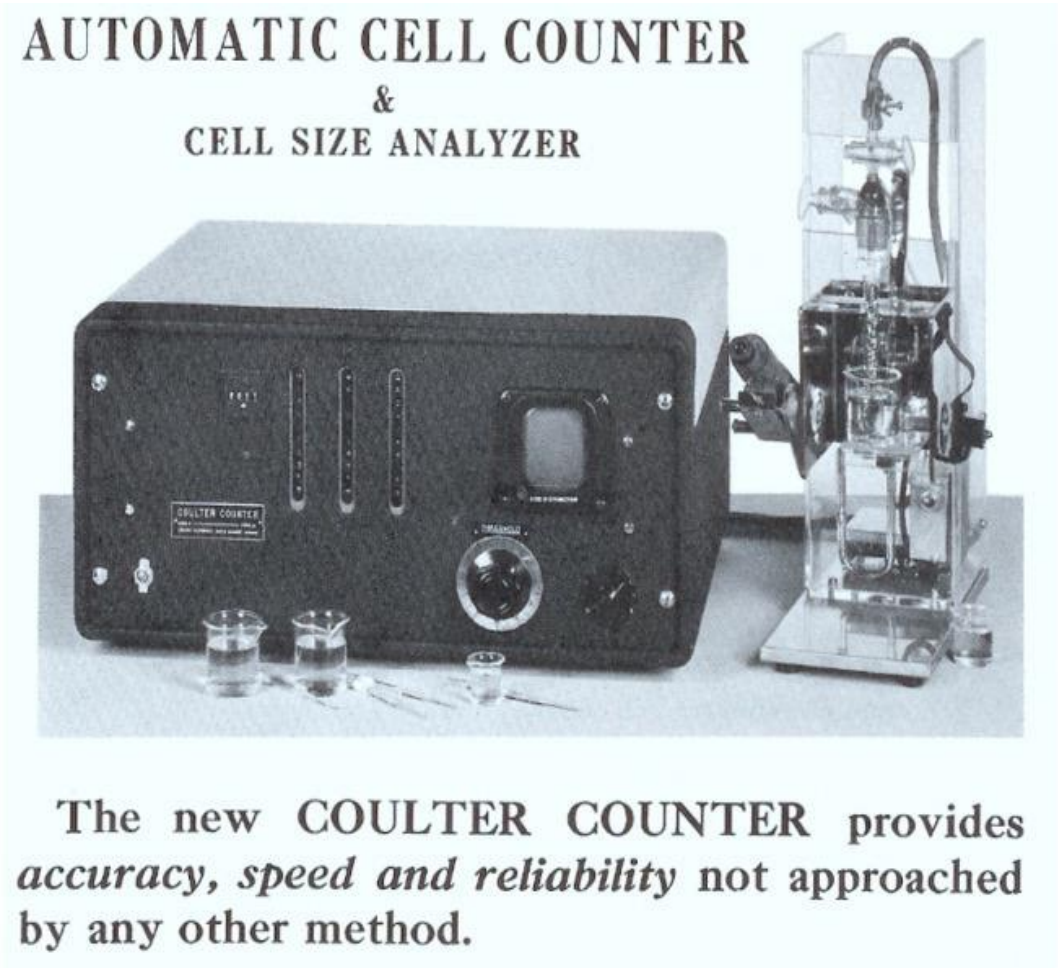
Diagnosis choice was improved

Information helps

And convenience counts!

4. THE RISE OF MACHINES
the psychology of our reactions

(with film references)



(a)

(b)

Cytometry Pt A, Volume: 83A, Issue: 5, Pages: 424-438, First published: 17 April 2013, DOI

Emotional response 1 – Machines are better than us

Image processing boundary shape detail (similar to humans)

Classify based on learning set to generate a set of cell forms (similar to humans)

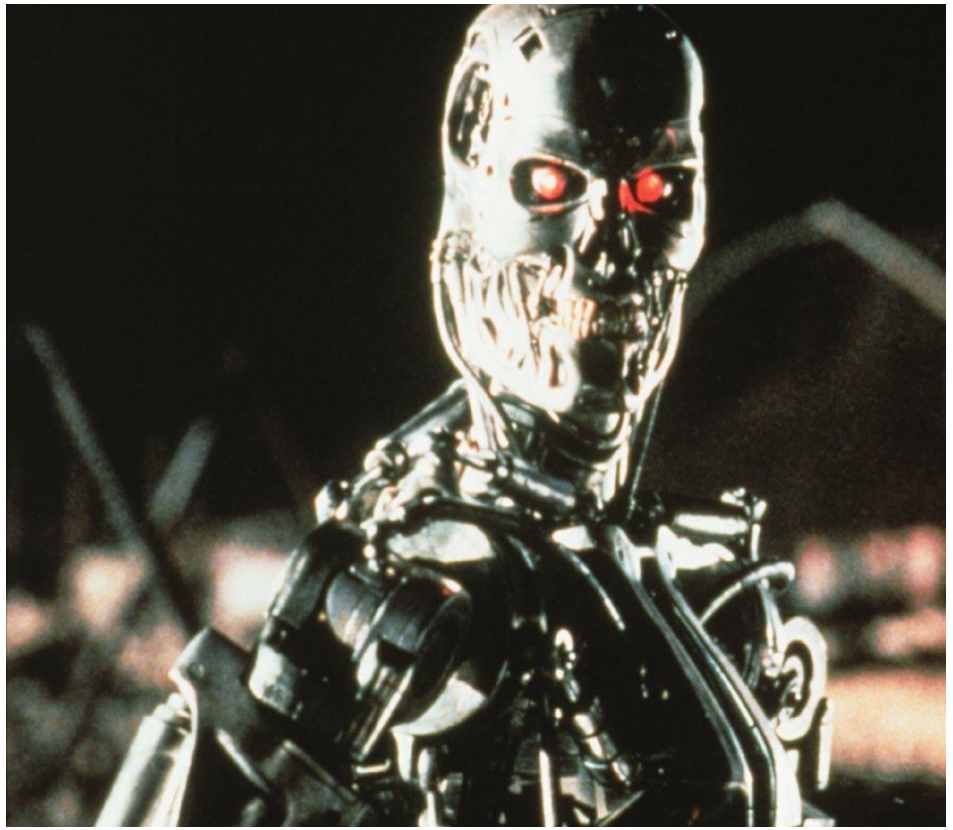
Use that set of features to suggest a diagnosis

Roy (NEXUS V replicant): “I've seen things... seen things you little people wouldn't believe”.

Is this true now – Will it be?

Emotional response 2: Machines can work harder

- Doesn’t need beaks
- Does not go home at the end of shift
- No emotional overlay and not subject to (human) bias



T1 terminator: “It doesn't feel pity, or remorse, or fear. And it absolutely will not stop... Ever”

Will this appeal to health service managers?

Could this help avoid bias?

Emotional response 3: it may process information better (well connected)

“Write a blood film report interpreting helmet cells, fragments, thrombocytopenia and anaemia”

Comments: Microscopic examination of the peripheral blood smear reveals several notable findings, which collectively suggest a complex hematological disorder:

1.RBC Fragmentation: The presence of numerous schistocytes, helmet cells, and microcytic, fragmented RBCs indicates mechanical injury to red blood cells within the microcirculation.

2.Anisocytosis and Poikilocytosis: Anisocytosis (variation in RBC size) and poikilocytosis (variation in RBC shape) are observed, consistent with ongoing hemolysis and anemia.

3.Helmet Cells: The presence of helmet cells is indicative of severe fragmentation of RBCs, likely due to shear forces encountered within small blood vessels.

4.Thrombocytopenia: The platelet count is reduced, suggesting thrombocytopenia. While not severely low, it may contribute to bleeding tendencies and the formation of small blood clots.

Interpretation: The blood film findings collectively suggest a condition characterized by microangiopathic hemolysis, thrombocytopenia, and anemia. This combination of findings can be seen in various clinical scenarios, including but not limited to:

SORT OF IMPRESSIVE BUT IS THIS REALLY GOOD?

1.Thrombotic Microangiopathies (TMA): Conditions such as thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS) are known TMAs. They are characterized by the formation of microthrombi in small blood vessels, which can lead to RBC fragmentation (schistocytes), thrombocytopenia, and hemolytic anemia.

2.Disseminated Intravascular Coagulation (DIC): DIC is characterized by widespread activation of coagulation, leading to the consumption of platelets and clotting factors. This can result in both thrombocytopenia and microangiopathic hemolysis.

3.Underlying Hematological or Systemic Diseases: Conditions such as autoimmune hemolytic anemia, paroxysmal nocturnal hemoglobinuria (PNH), and malignancies may also present with similar blood film findings in some cases.

Further evaluation, including additional laboratory tests, clinical history, and imaging studies, is essential to determine the underlying cause and guide appropriate treatment for the patient. Timely diagnosis and management are critical to address the complex nature of this hematological disorder. Consultation with a hematologist is highly recommended for further assessment and diagnosis.

Emotional response 4 Can we trust machines

“Ginny!" said Mr. Weasley, flabbergasted. "Haven't I taught you anything? What have I always told you? Never trust anything that can think for itself if you can't see where it keeps its brain?”

Machine bias?

Using this same image….

[illegible] here (from Portugal)

My view

Don’t be afraid, but be critical
What is it for?
It may help reduce knowledge errors
It may help reduce heuristic errors
We should always value decision support – both information and cell recognition and this may help
Should not be used as person replacement solely for cost saving or convenience

Will it improve outcomes for patients?

Thanks to …..

- Staff in haematology at Manchester over many years
- Michelle Brereton
- UK NEQAS staff and participants
- All those who enjoy morphology
- People who believe in free access to images for education