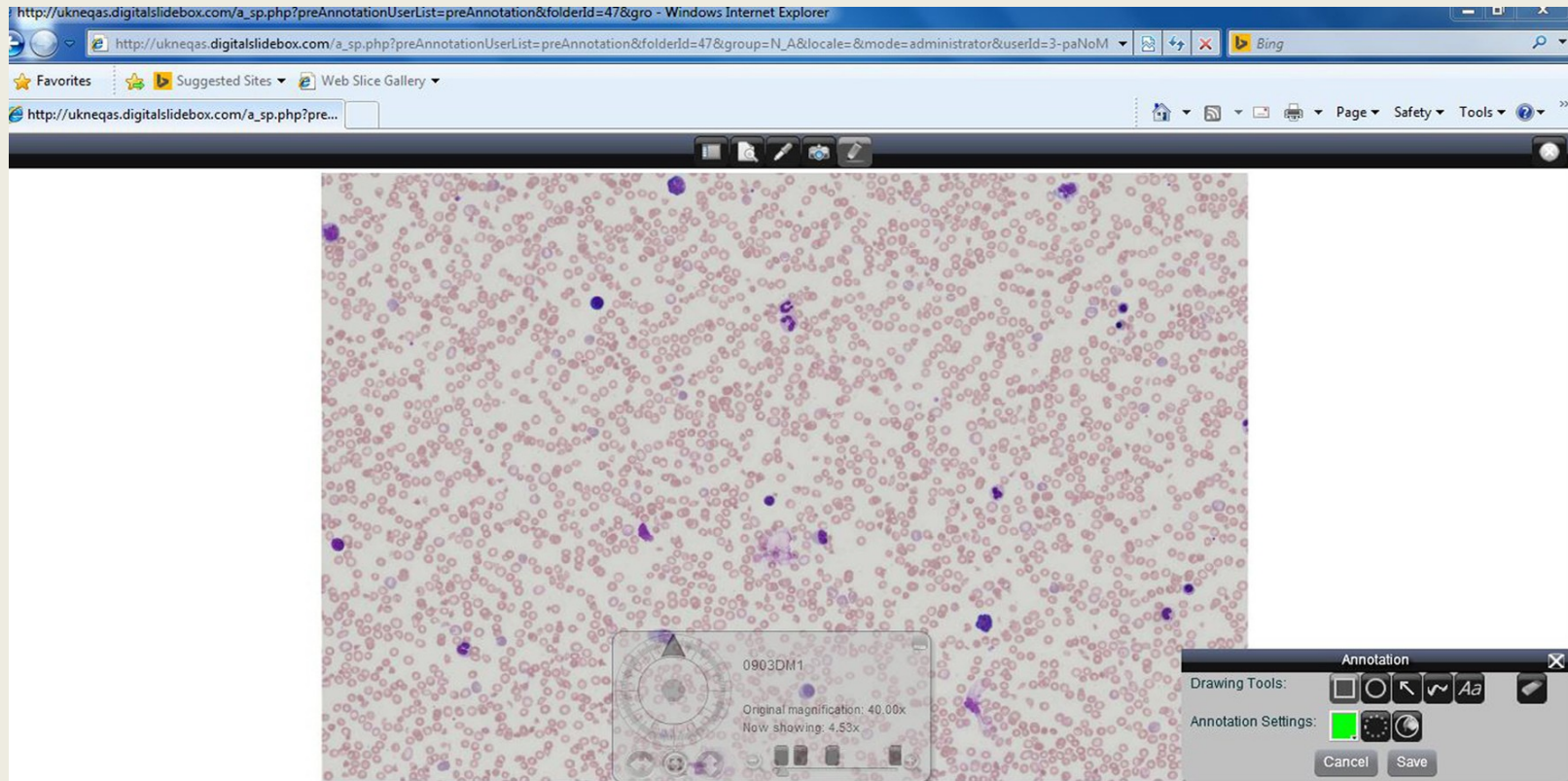


Why do we make mistakes in
morphological diagnosis – how can
we improve?

Michelle Brereton & John Burthem
Manchester, UK

UK NEQAS(H) DM scheme

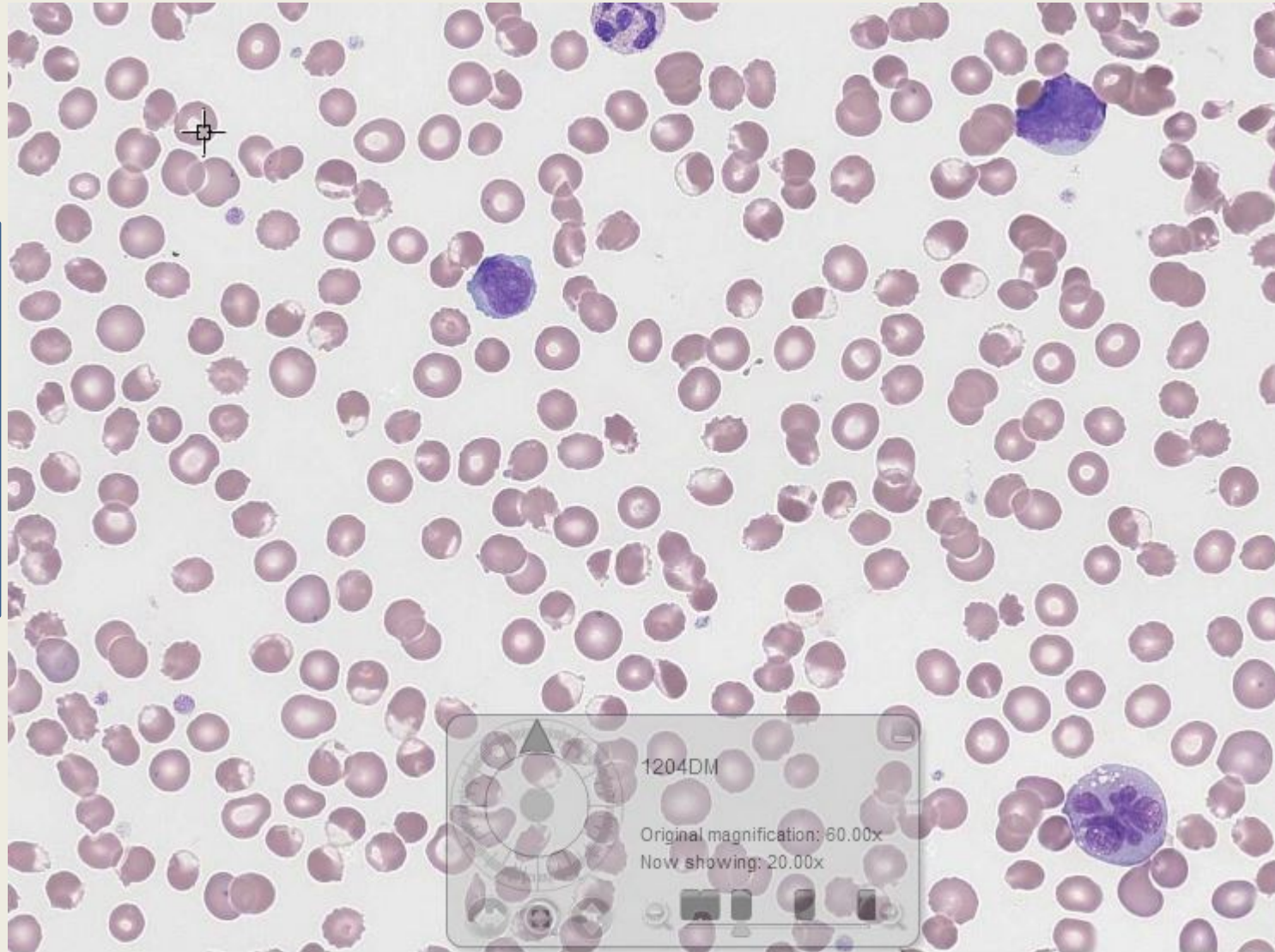


1. Select up to 5 significant morphological features from a defined list
2. Place these in priority order 1-5
3. Answer multiple choice question : “what would I do next?”
4. Offer free text opinion generally: “what is your preferred diagnosis?”

But some people get the answers wrong!

Are we really helping this group sufficiently?
Do we really know why they get things wrong?

Analysing morphology is more complex than we think



14/320

4000

20000

Slide overview



Digital Slide Box - A Slidepath Software Solution

http://dsbdev.slidepath.com/preAnnotate.php?slideId=7285

Select Slide View Options View Tools

Slide overview

X:19 Y:41
Mag: 26x

Windows taskbar: start, Digital Slide Box - A Sl..., Microsoft PowerPoint ... EN 51% 06:06

This screenshot shows the main interface of the Digital Slide Box software. The central area displays a microscopic image of cells. A navigation toolbar is located at the bottom of the image area, featuring directional arrows, a zoom slider, and a status box showing coordinates (X:19, Y:41) and magnification (Mag: 26x). A 'Slide overview' inset in the top right corner provides a grid-based overview of the slide content. The software is running in a web browser window, with the Windows taskbar visible at the bottom showing the 'start' button and several open applications.

All

Slide overview

X:34 Y:4
Mag: 20x

Windows taskbar: start, Digital Slide Box - A Sl..., Microsoft PowerPoint ... EN 49% 06:05

This screenshot shows a smaller version of the Digital Slide Box interface, likely a thumbnail or a secondary window. It features the same microscopic image, navigation toolbar, and 'Slide overview' inset as the main window. The status box at the bottom of the image area shows coordinates (X:34, Y:4) and magnification (Mag: 20x). The Windows taskbar at the bottom indicates the software is running alongside other applications, with the system tray showing 49% battery and the time 06:05.

Can we analyse our data to see why we arrive at incorrect answers?

The Heuristic Approach: “Fast and Frugal”

A model to understand how people arrive at a morphological opinion

1. Familiarity/unfamiliarity
2. Recognition
3. Classification
4. Reinforcement
5. Priority assignment
6. Interpretation
7. Action

We all use these approaches (1)



A simple case

We all use these approaches (2)



A complex case

We all use these approaches (2)



Made the evidence fit my view = Framing effect bias

Persisted in original view = anchoring bias

Simplification = multiple alternatives bias

Stopped looking or thinking = Satisfaction of search (premature closure)

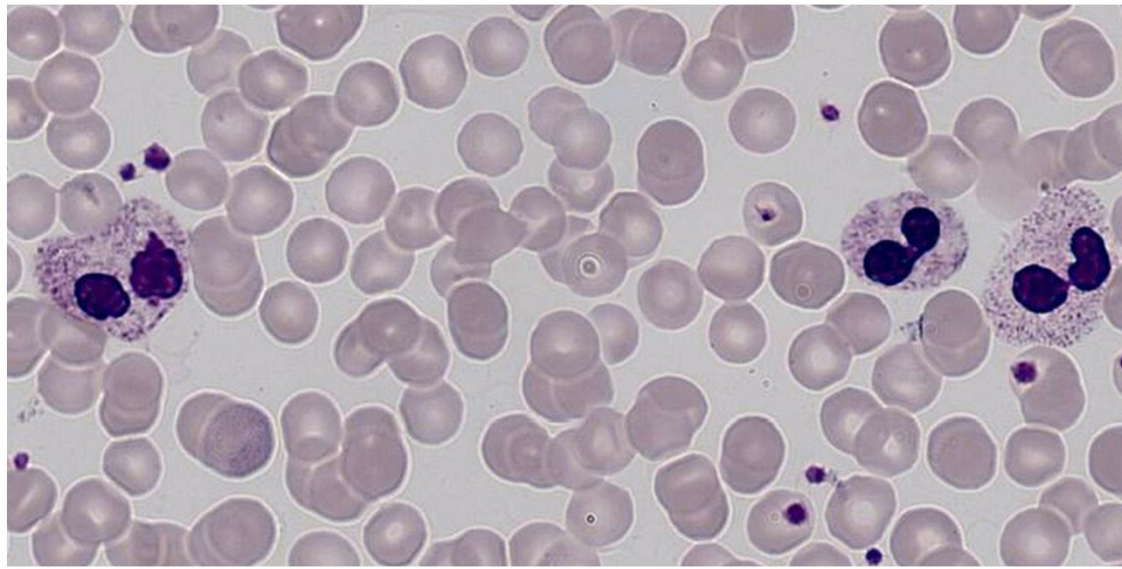
Heuristic approaches can introduce major sources of bias!

CASE 1 and 2

Simple cases

CASE 1

Inherited Pelger Huet anomaly Overview of features



A routine pre-operative blood sample reveals these features on the film.

Preferred answer:

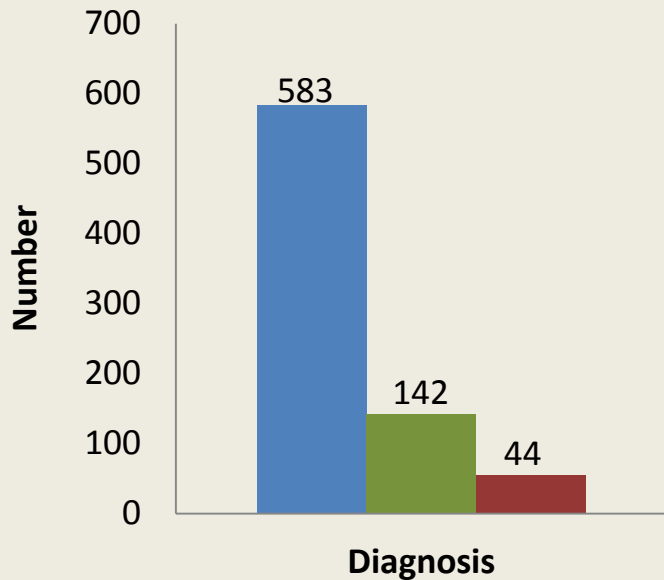
1. Pelger cells +/- other normal features
2. Pelger cells ranked most important
3. Action: low priority action
4. Diagnosis: Pelger Huet anomaly

CASE 1

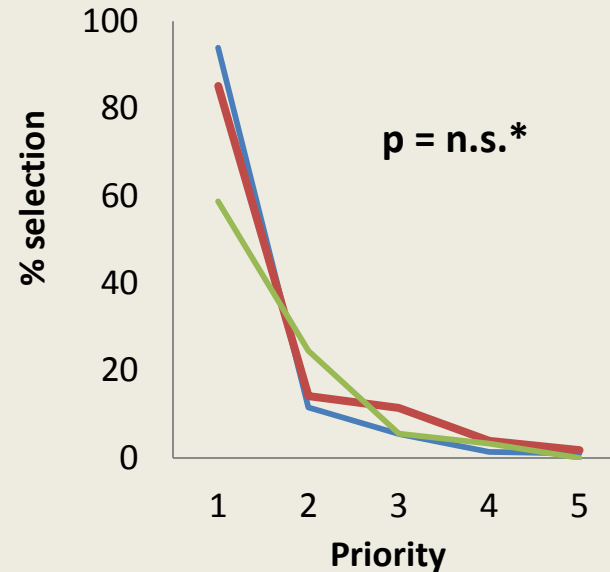
Inherited Pelger Huet anomaly Overview of selected features

Participants completing all aspects of survey: 1029

Major distinct diagnostic groups



Priority given to neutrophil features

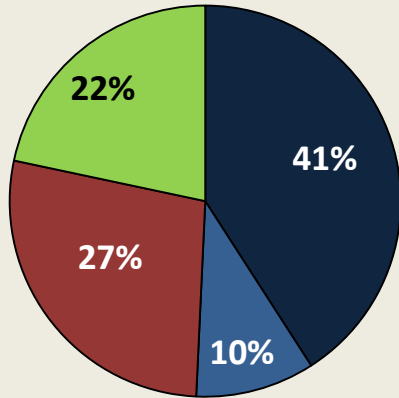


■ Pelger Huet anomaly ■ Myelodysplasia ■ Reactive changes

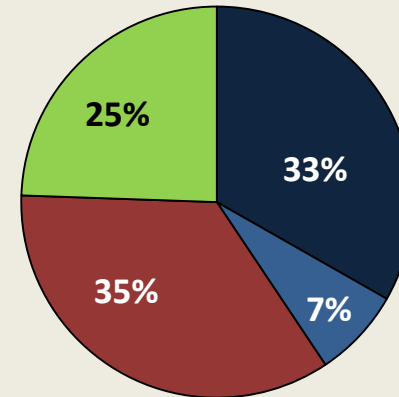
*Chi Square test two tailed (Fisher's exact)

CASE 1

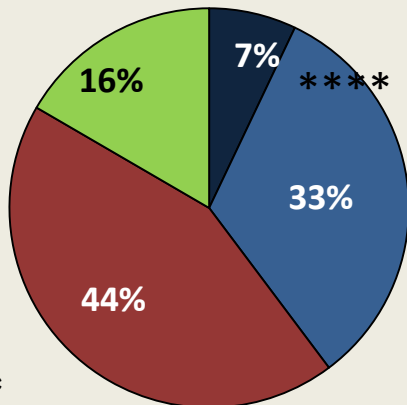
Selected features and final diagnosis



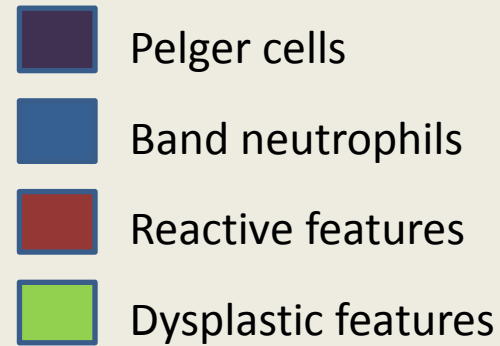
Pelger Huet



Myelodysplasia



Reactive

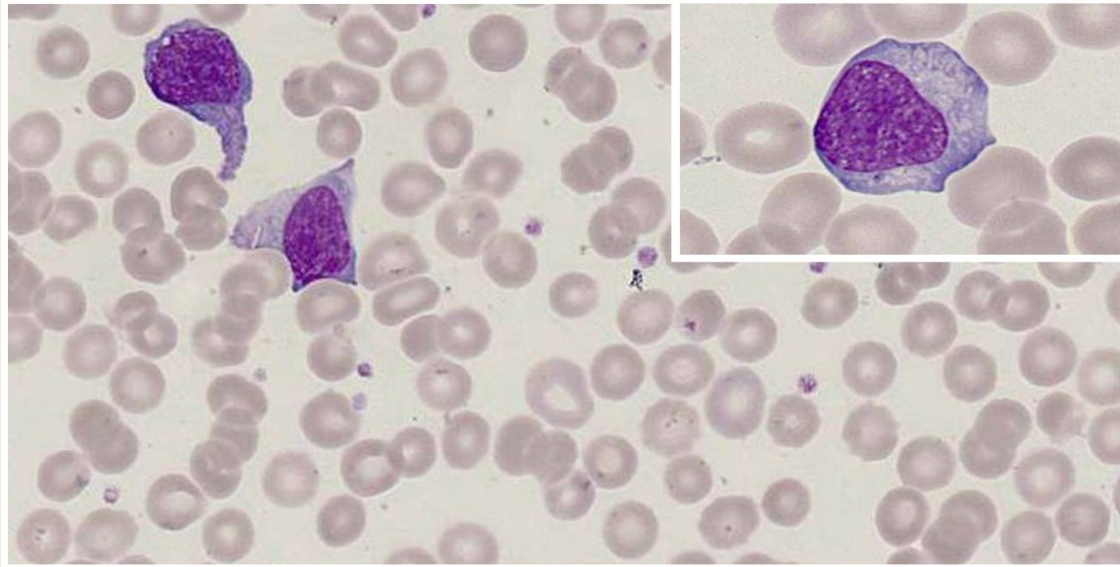


Chi Square Test two-tailed (Fisher's exact)

CASE 2

Reactive lymphocytes in glandular fever

Overview of features



A young man presenting with enlarged neck lymph nodes.

Preferred answer:

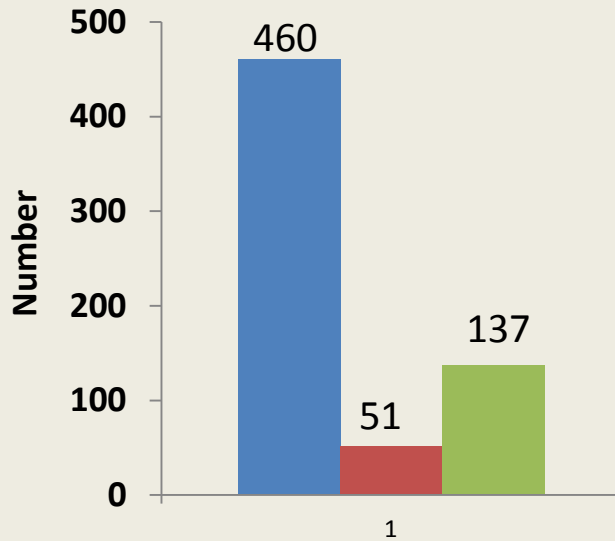
1. Reactive lymphocytes (one or more choices)
2. Reactive lymphocytes ranked most important
3. Action: low priority action
4. Diagnosis: Reactive viral (?EBV)

CASE 2

Reactive lymphocytes (glandular fever) Overview of selected features

Participants completing all aspects of survey: 713

Distinct diagnostic groups

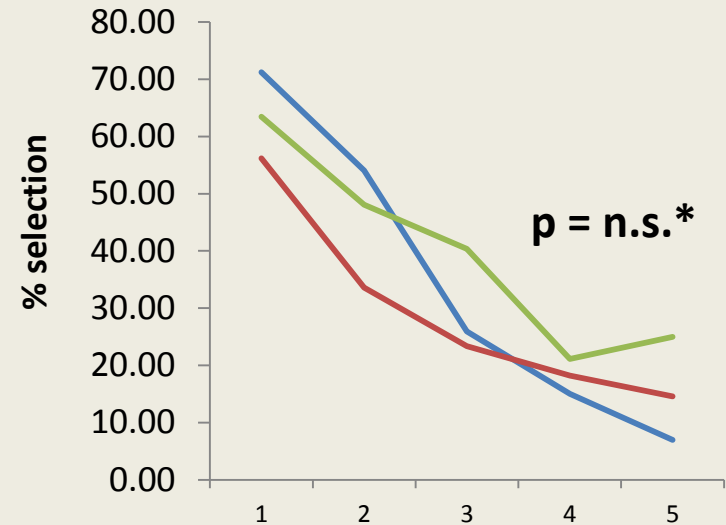


Features of viral infection

Viral infection exclude neoplasia

Neoplastic cells

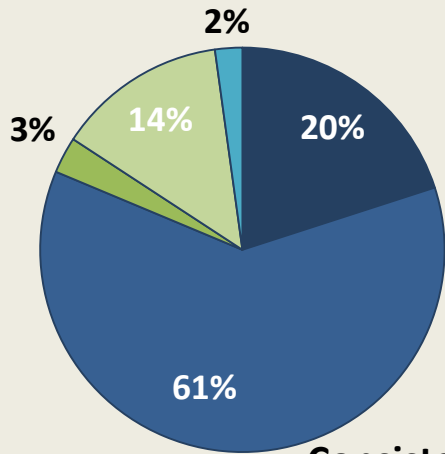
Priority given to lymphocyte features



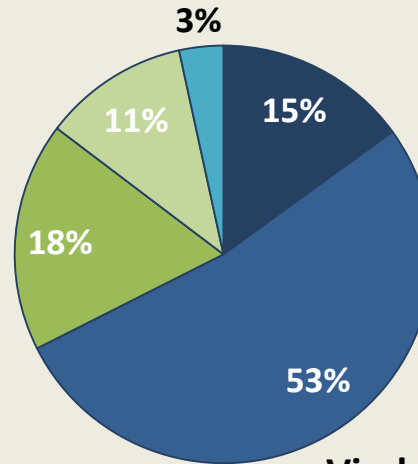
*Chi Square test two tailed (Fisher's exact)

CASE 2

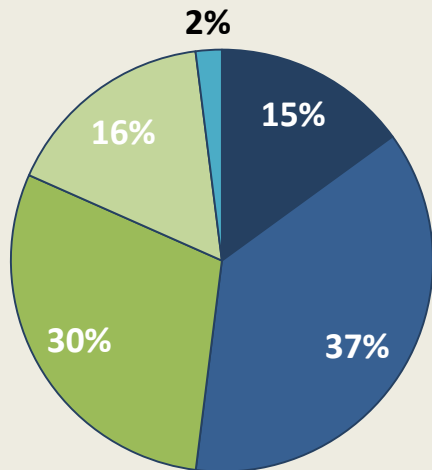
Selected features and final diagnosis








Consistent with viral infection



Viral infection, exclude neoplasia

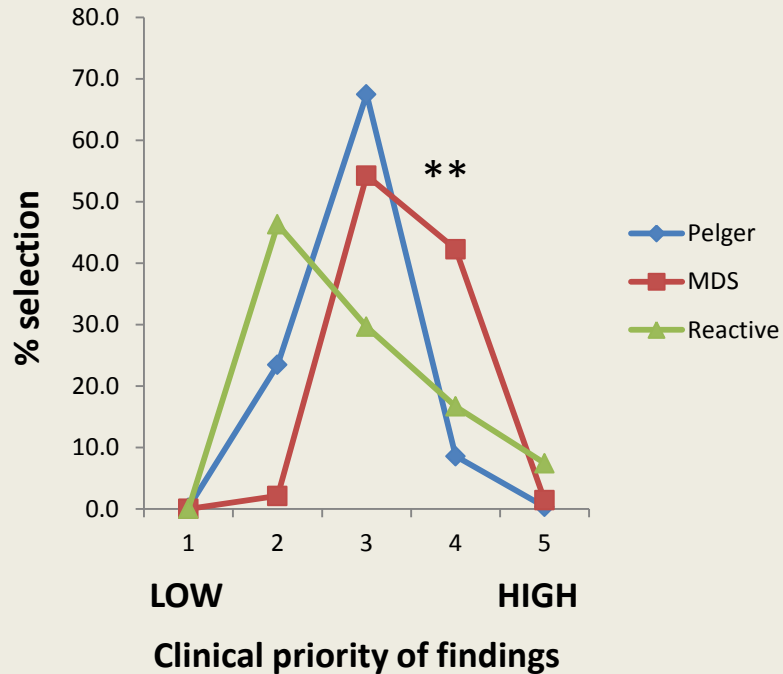


Neoplastic

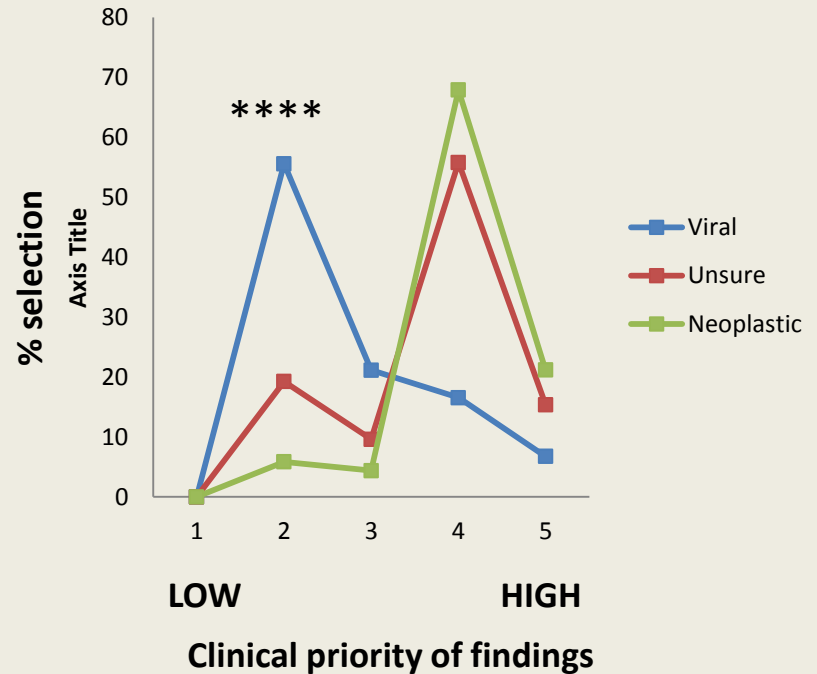
-  Lymphocytosis
-  Reactive lymphocytes
-  Neoplastic lymphocytes
-  Supports neoplastic
-  Supports reactive

CASES 1 and 2

Why be interested?



CASE 1
(Pelger Huet anomaly)



CASE 2
(Viral infection)

** p<0.001
**** p<0.00001
Mann Witney U test

CASES 1 and 2 Principle sources of error

In these cases interpretation depended predominantly on accurate assessment of a single abnormal cell

Analysis

Familiarity, recognition and prioritisation: well completed irrespective of diagnosis

MAJOR ERROR SOURCE:

Classification: recognising the abnormal cell

Substantial contributions:

Framing effect (overstating supportive features)

Anchorage (ignoring lack of support)

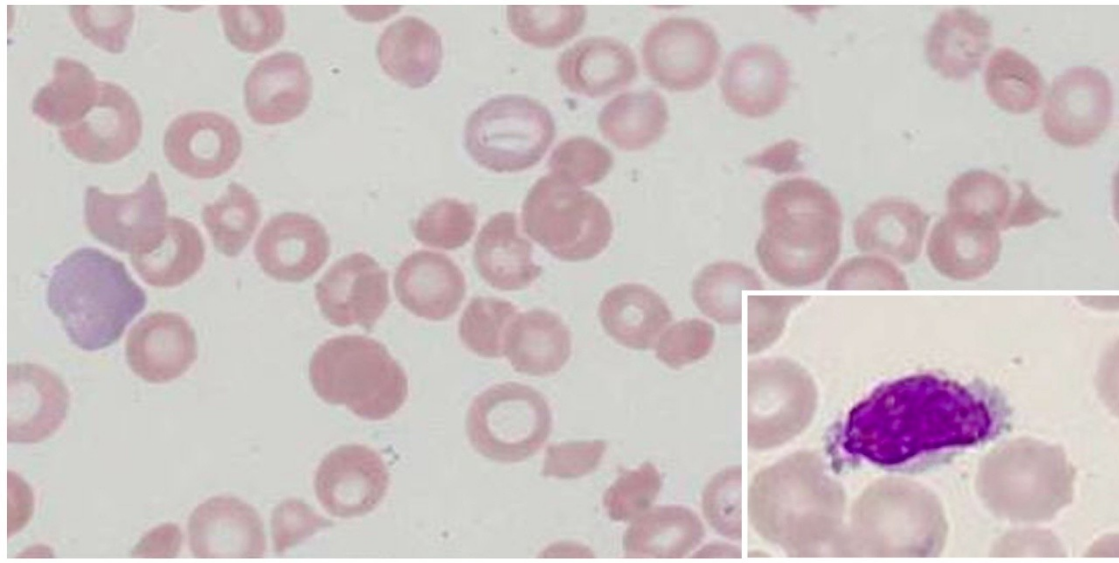
NOTE The highly significant effect on action/outcome

CASE 3

Complex morphology unifying diagnosis

CASE 3

Microangiopathic haemolysis (TTP) with acute viral infection (HIV)



A patient attending an evening clinic is unwell

Preferred answer:

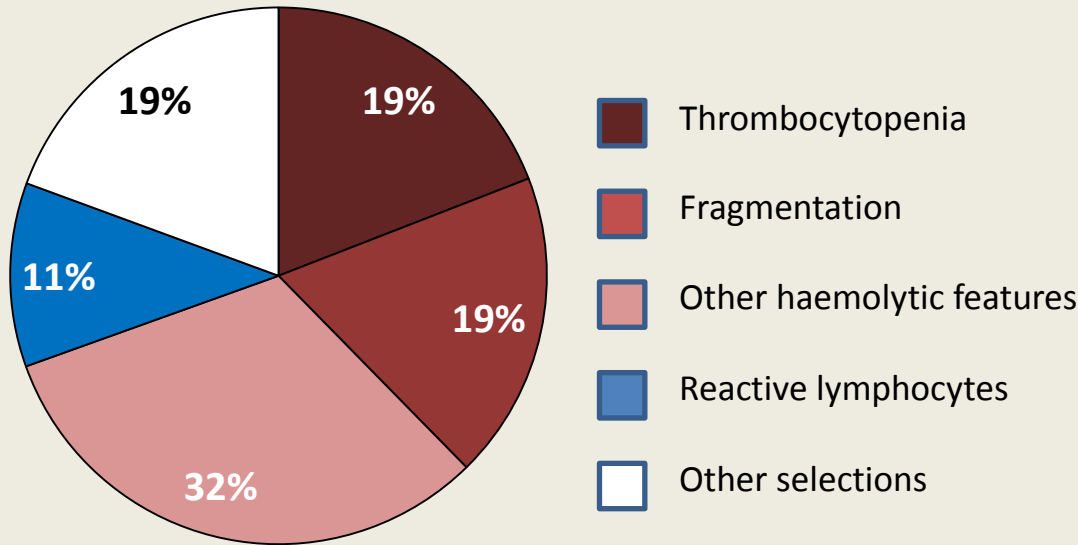
1. Thrombocytopenia, Fragmentation features, general haemolysis features
2. Thrombocytopenia and fragmentation ranked most important, reactive lymphocytes recorded
3. Action: High priority action
4. Diagnosis: Microangiopathic haemolysis +/- viral infection

CASE 3

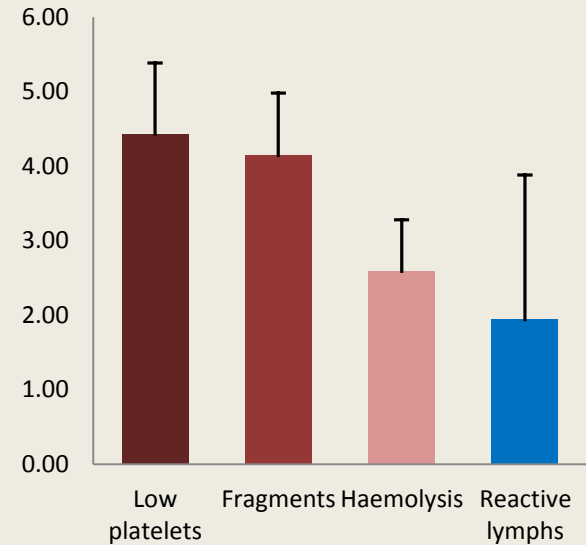
Thrombotic thrombocytopenic purpura with acute HIV Overview of selected features

Participants completing all aspects of survey: 751

Feature choice



Feature priority



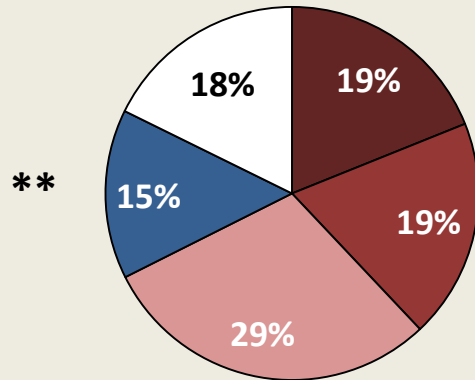
Preferred diagnosis:

Microangiopathic haemolysis (MAHA)	381	(51%)
MAHA and viral illness	125	(16%)
Haemolysis unspecified	155	(21%)

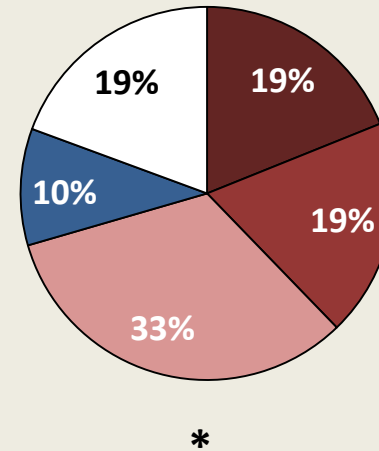
CASE 3

Selected features and final diagnosis

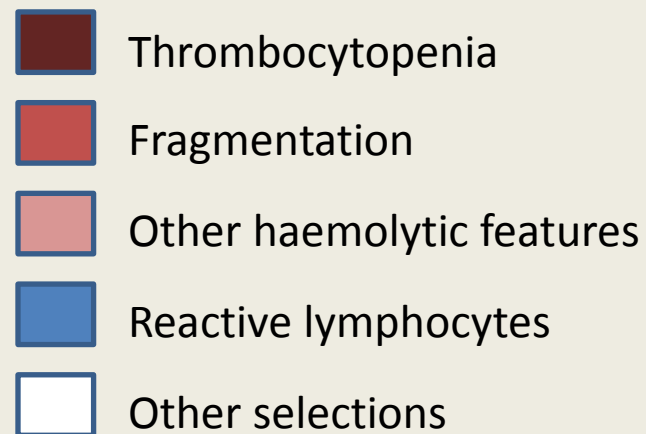
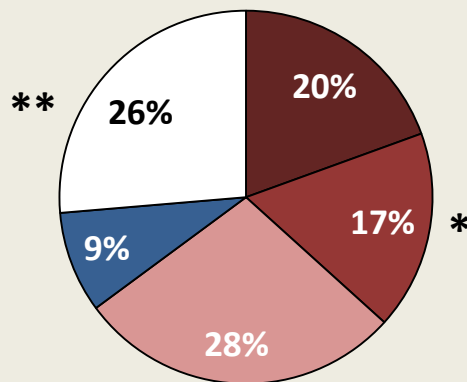
MAHA and viral illness



MAHA alone

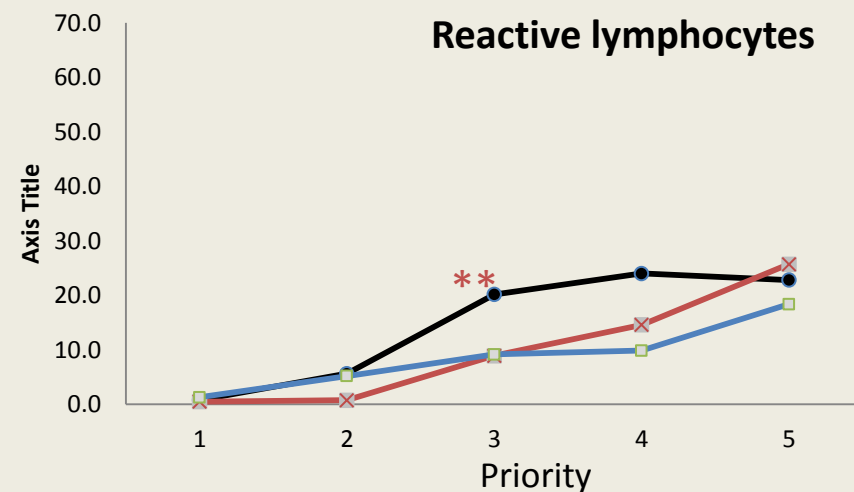
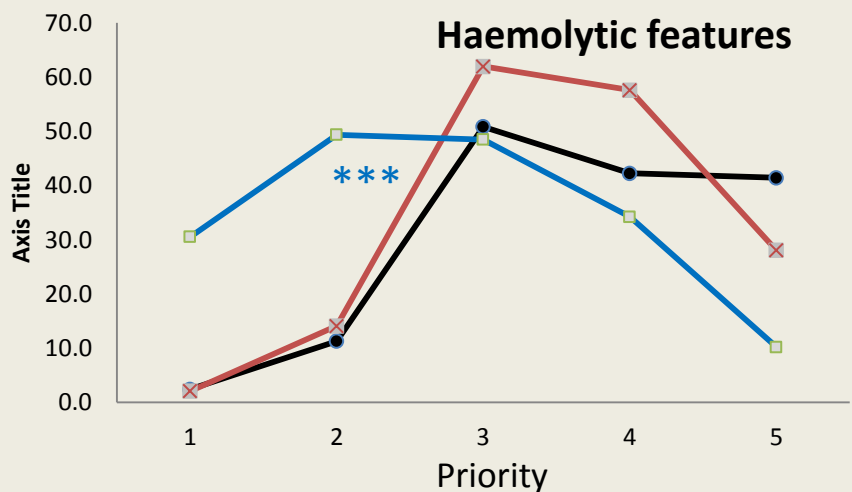
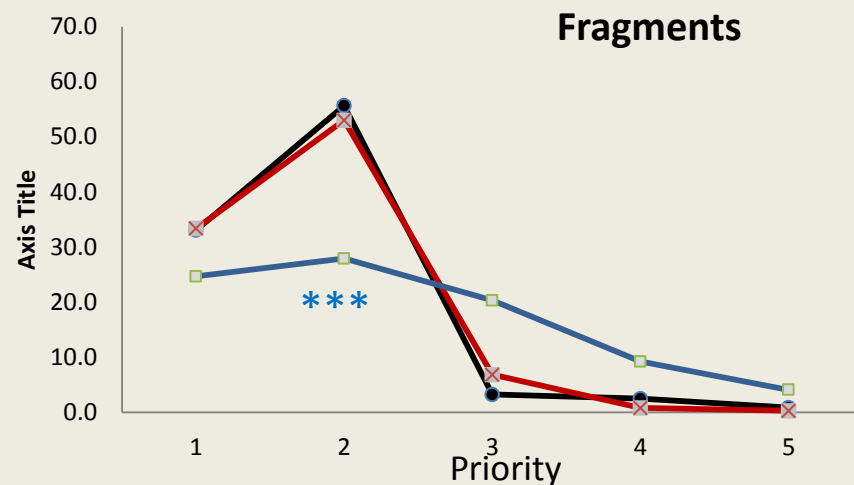
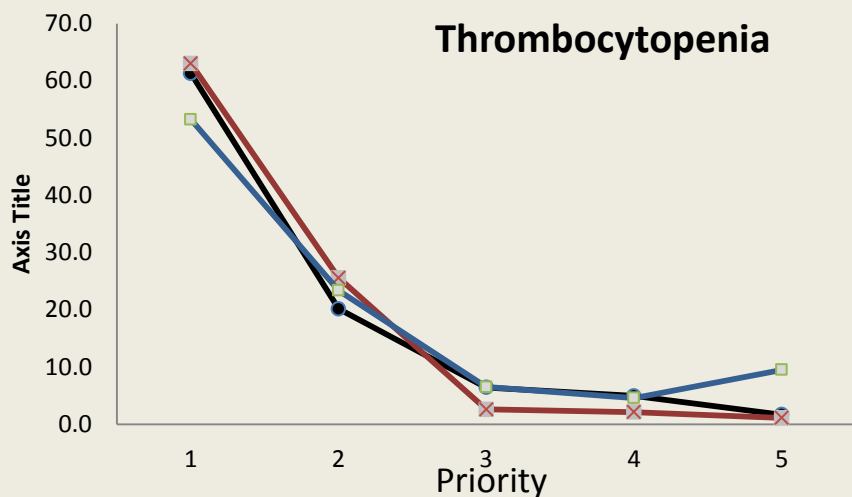


Haemolysis other



*p<0.01
** p<0.001
Chi Square test

CASE 3 Priority assigned to features according to preferred diagnosis



TTP & viral

TTP only

Haemolysis

** p<0.001
 *** p<0.0001
 Mann Witney U test

CASE 3 Elements governing diagnostic conclusion

Interpretation

Feature selection was remarkably similar **BUT** diagnosis differed

MAJOR ERROR SOURCE:

Prioritisation (confirmation bias – emphasising features that fit)

Simplification (multiple alternatives bias and elimination by aspects)

Possible contribution:

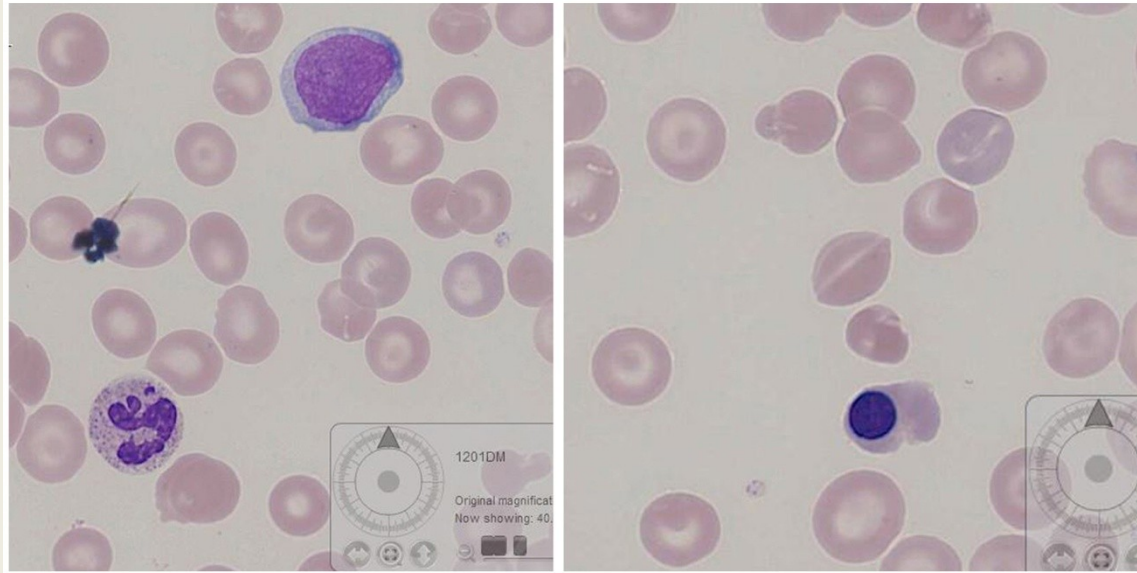
Premature completion (I have a diagnosis, I can finish looking)

CASE 4

Complex case – dual pathology

CASE 4

HbSC disease with acute myeloid leukaemia

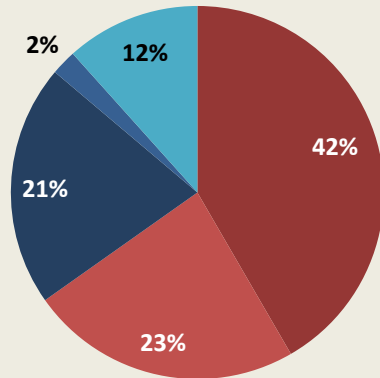


A patient under long-term follow up as an out patient clinic has changed blood count features.

Preferred answer:

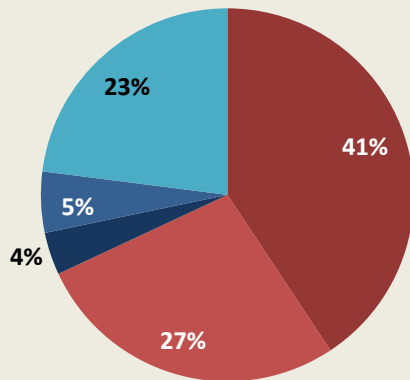
1. Blast cells and features of haemoglobinopathy (HbC or HbSC)
2. Blast cells ranked most important, red cell features recorded
3. Action: high priority action
4. Diagnosis: acute leukaemia with haemoglobinopathy

Acute myeloid leukaemia selected (n= 162)



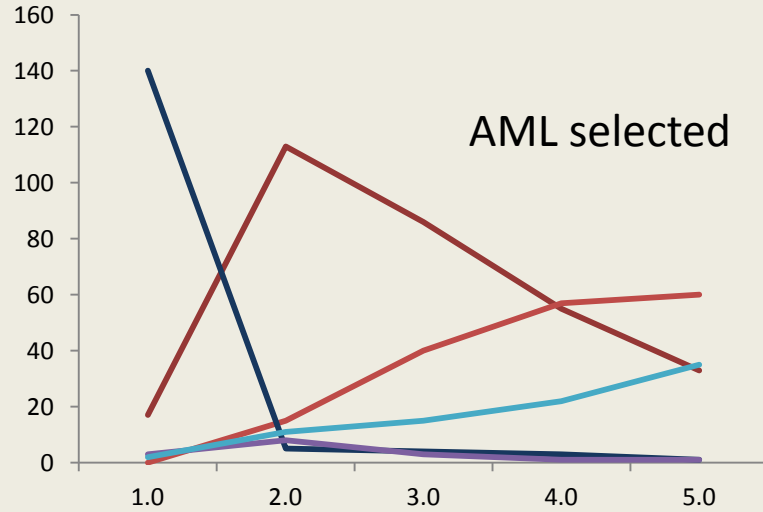
- Haemoglobinopathy features
- Other red cell features
- Blast cells
- Other white cell types
- Other white cell features

Reactive white cells selected (n= 90)

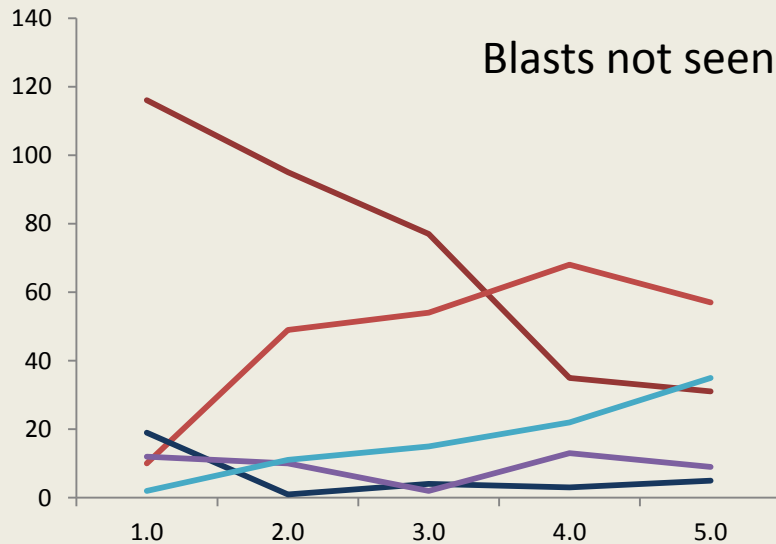


CASE 4

HbSC disease with acute myeloid leukaemia

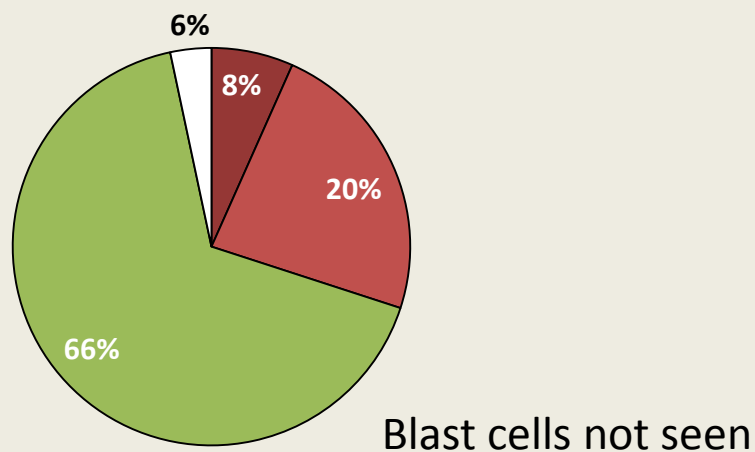
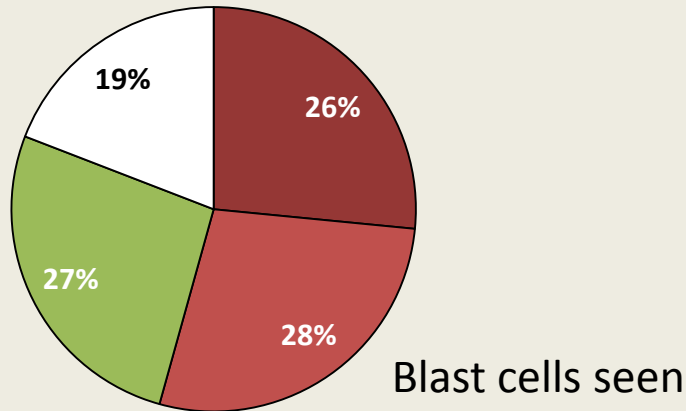


- Haemoglobinopathy features
- Other red cell features
- Blast cells
- Other white cell types
- Other white cell features

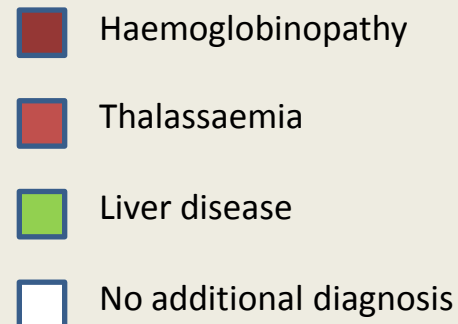


CASE 4

HbSC disease with acute myeloid leukaemia



How did the perception of red cell and white cell findings relate to the perception of white cells?



CASE 4 Elements governing diagnostic conclusion

Interpretation

This did not appear to be a classification error or prioritisation error, those making an incorrect diagnosis simply failed to see the blast cells!

MAJOR ERROR SOURCE:

- Multiple alternatives bias (simplified to exclude other important features)
- Framing effect (substantial influence of other features)
- Premature closure (arriving at a single diagnosis and stopped)

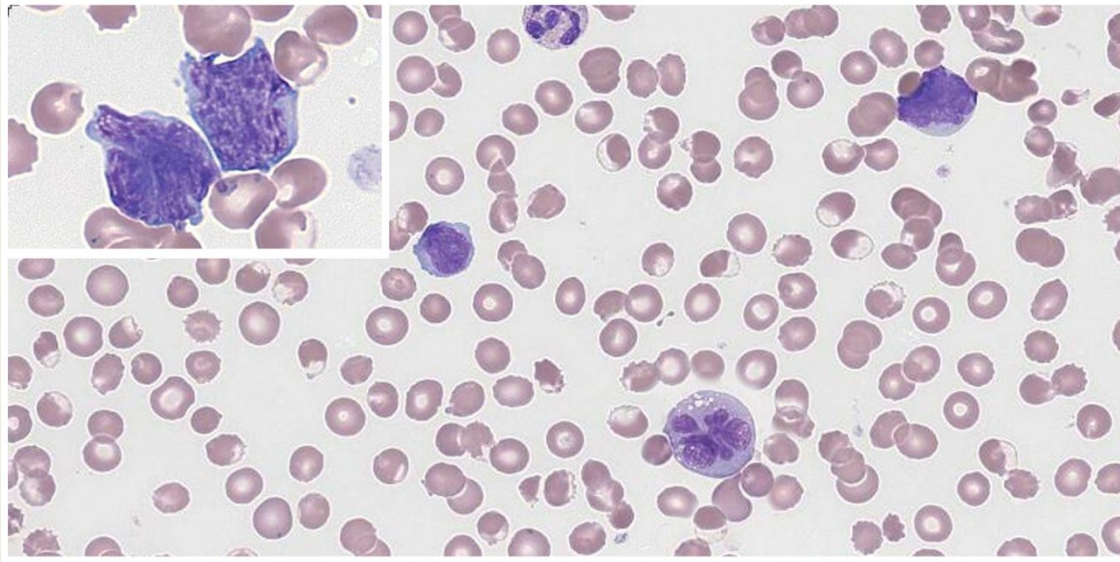
What are the Heuristic techniques in diagnosis

TECHNIQUE	BENEFITS	DISADVANTAGES
Availability	Applying a context can improve speed and accuracy	May reduce the detection of less common disorders
Classification	Enhances speed, improves accuracy, interpretive framework	Incorrect classification affects all subsequent action
Reinforcement (framing)	Assists interpretation and improves accuracy	May falsely reassure
Prioritisation	Simplification: helps speed and the accuracy of interpretation	If incorrect affects interpretation
Simplification	Allows rapid processing of complex datasets	If incorrect affects interpretation
Completion of search	Essential to speed	Premature completion misses diagnoses

CASE 5

Does experience help?

CASE 5 Oxidative haemolysis and Adult T-cell Leukaemia Lymphoma



An man receiving medical treatment becomes unwell.

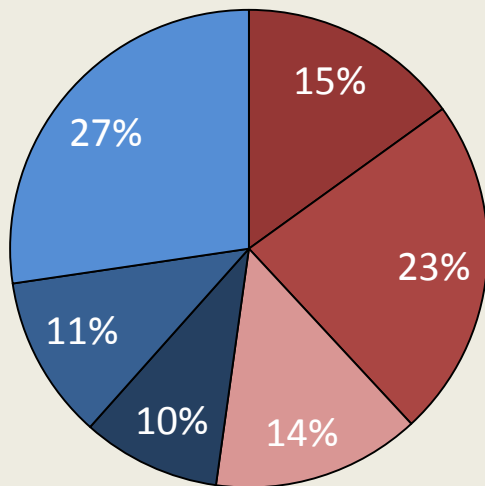
Preferred answer:

1. Oxidative haemolysis with neoplastic lymphocytes
2. Oxidative haemolysis ranked most important
3. Action: high priority action
4. Diagnosis: Oxidative haemolysis (G6PD def) plus neoplastic lymphocytes or blasts

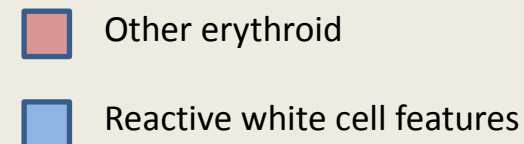
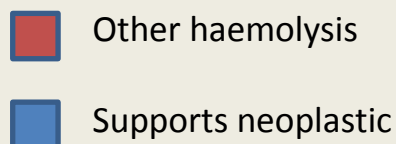
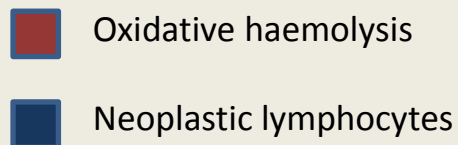
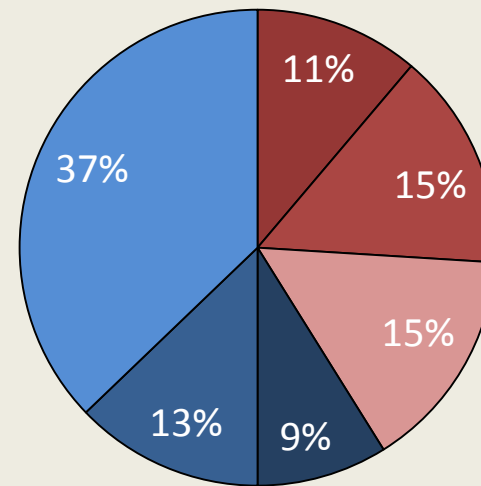
CASE 5 Oxidative haemolysis and Adult T-cell Leukaemia Lymphoma

FEATURE SELECTION

UBMS



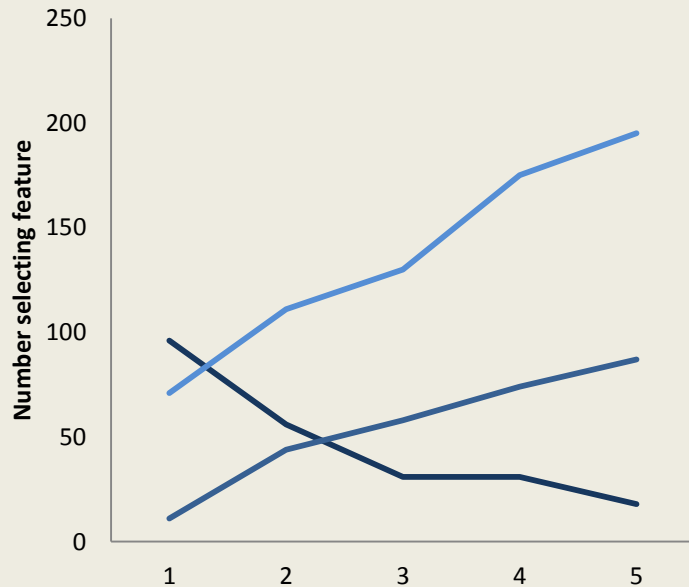
NRBMS



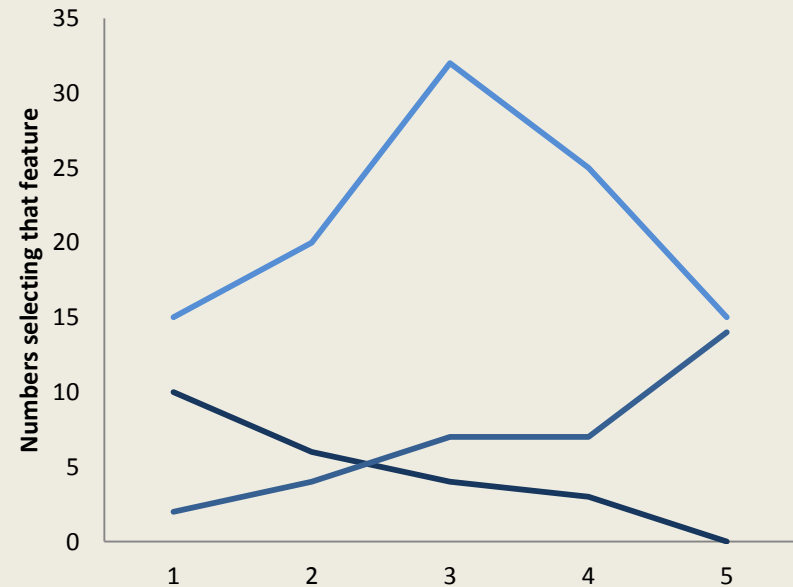
CASE 5 Oxidative haemolysis and Adult T-cell Leukaemia Lymphoma

FEATURE Prioritisation

UBMS



NRBMS



Neoplastic lymphocytes

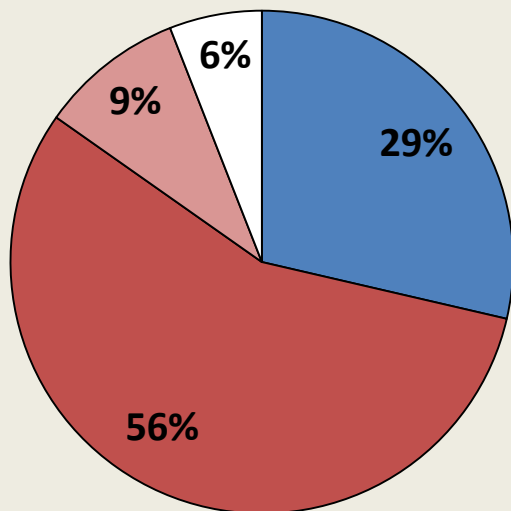
Supports neoplastic

Reactive white cell features

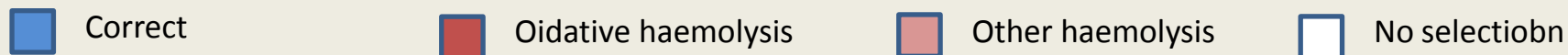
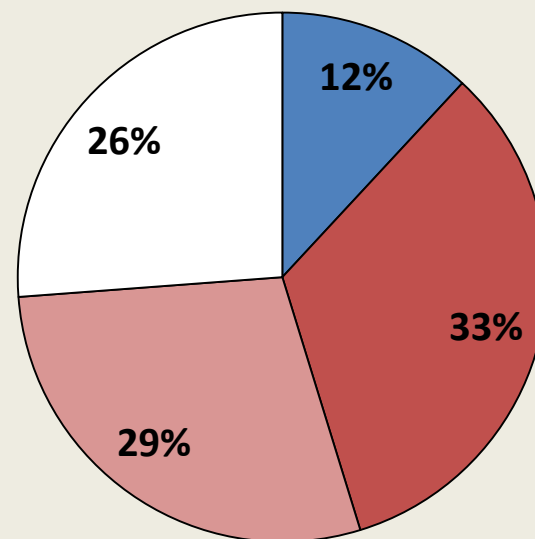
CASE 5 Oxidative haemolysis and Adult T-cell Leukaemia Lymphoma

DIAGNOSIS CHOICE

UBMS



NRBMS



Conclusions

1. The nature of errors depends significantly on the complexity of morphological features
2. In “simple” cases, where there is a single feature diagnosis depends **mainly** on the classification of that feature
3. As cases become more complex, heuristic techniques play a much greater role in interpretation **but also produce specific patterns of errors**
4. Experience improves the application of these techniques (but does not eliminate errors)
5. Action may be very strongly influenced by the choices made

Strategies to improve interpretation

- AWARENESS OF SOURCES OF ERROR
- STANDARDISATION (ICSH)
- GUIDANCE ON REPORT STYLE
- ASSESSMENT: competency
- DECISION SUPPORT: tools

Acknowledgements

Keith Hyde, Barbara De la Salle, Dan Pelling, UK NEQAS

UK NEQAS(H) DM participants

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Manchester University

Leica-SlidePath