Higher Specialist Diploma

Haematology

Examination – September 2021

Short-answer questions

60 minutes

Attempt all four questions

Instructions to candidates

1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

2. Record your candidate number, the question number and the page number in the spaces provided on the answer sheets

3. Begin each new answer on a new page

4. Each question is worth 25 marks

1. You are informed by the recently qualified biomedical scientist, that the normal and abnormal QC has failed on both your haematology analysers this morning. The controls were fine when tested yesterday morning, and the normal QC was within limits when it was tested yesterday evening. What actions would you take?

2. Your latest blood coagulation EQA report is shown below. Discuss these results, and outline further investigations (if any) you may take, justifying your decision

Assay	**FVIII**	**FIX**
Sample No	21/24	21/25
Your method	1-stage APTT	1-stage APTT
Your reagent	Il SynthasIL	Il SynthasIL
Your result	**15.0**	**40.0**
Units	u/dl	u/dl
Your normal range	50-150	50-150
Participants (n)	350	250
Median result (u/dl)	**30.0**	**36.0**
Your % deviation	-50.0	11.1
Z-score	-3.5	1.4
Performance grade	e	D
Cumulative grades	e/e/e	D/e/D
Cumulative performance	Persistently outwith consensus	Persistently outwith consensus
Your interpretation	Abnormal	Borderline
Overall interpretations		
Normal	0.5%	4.5%
Borderline	1.5%	14.5%
Abnormal	98.0%	81.0%

3. Your laboratory manager has asked you to evaluate performance of a new haematology analyser. Briefly outline how would you plan to do this.

4. Your lab manager has asked you to prepare a presentation for band 5 BMSs on pre-analytical variables and their effects on results. Describe the key points you would make in your presentation.

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Essay Paper

120 minutes

Attempt 2 out of 5 questions

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1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

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3. Begin each new answer on a new page

4. Each question is worth 100 marks

1. Evaluate how the recognition and identification of atypical intracellular organelles and inclusion bodies can inform diagnostic decision making in the routine haematology laboratory.

2. Evaluate the contribution of automated red cell parameters to the diagnosis and monitoring of anaemia.

3. Discuss how clinical and laboratory data are used in the diagnosis and classification of myelodysplastic syndromes.

4. Critically compare genetics/genomics with functional assays in the investigation of platelet disorders.

5. Critically discuss alternative anticoagulant therapies to warfarin, and the challenges these therapies pose to the haemostasis lab.

Higher Specialist Diploma

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Case studies

120 minutes

Attempt all case studies

Instructions to candidates

1. Record your candidate number and HSD discipline on the front sheet of the answer booklet

2. Record your candidate number, the question number and the page number in the spaces provided on the answer sheets

3. Begin each new answer on a new page

4. Each question is worth 100 marks

5. For these case study questions you are strongly advised to answer the questions as they arise during the case study to avoid later information impacting adversely on your answers to the earlier questions by presuming an "outcome".

SEEN CASE STUDY

1.
A 69-year-old male, presents to his GP feeling unwell. His pulse rate is 124 and he feels short of breath. He reports pallor and lethargy over the last week or two.

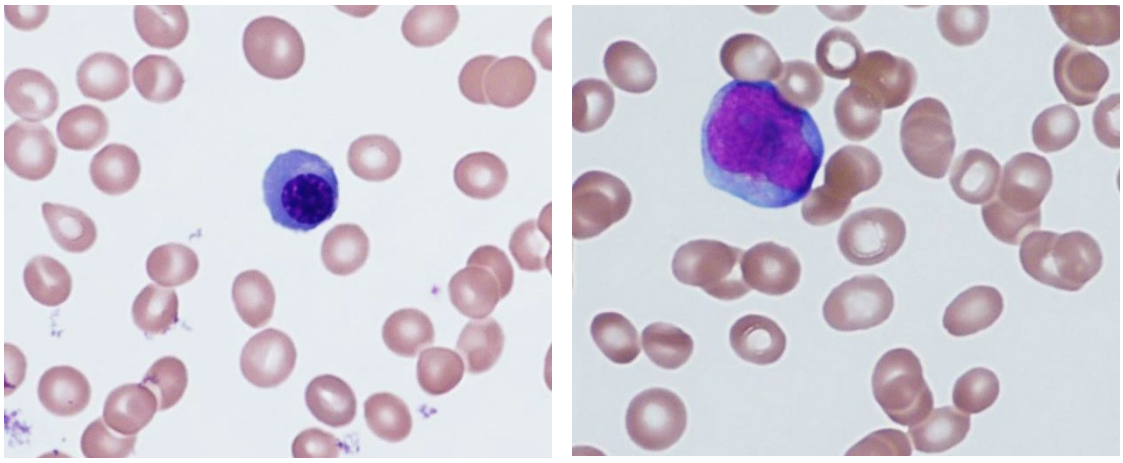
Table 1: Initial Full Blood Count Investigations

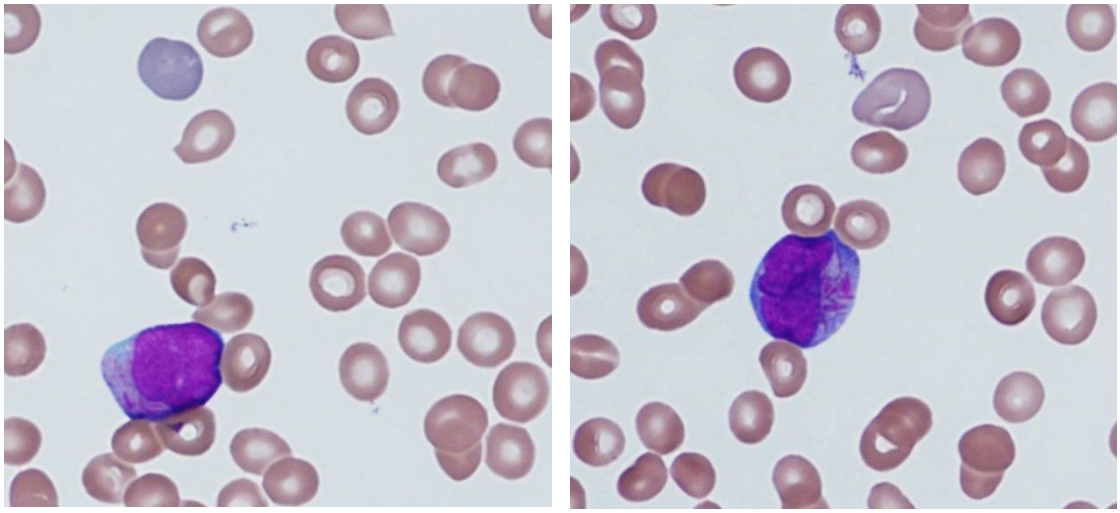
Full Blood Count		
	Result	**Reference Range**
White Blood Cell count ($x10^9$/L)	0.9	4.0-11.0
Haemoglobin (g/L)	66	120-170
Platelets	9	150-450
Red cell count ($x10^{12}$/L)	1.83	4.3-5.7
Haematocrit	0.177	(0.37-0.51)
Mean Cell Volume (fL)	96.4	80-100
Neutrophils ($x10^9$/L)	0.4	2.0-7.0
Lymphocytes ($x10^9$/L)	0.4	1.0-3.0
Monocytes ($x10^9$/L)	0.0	0.2-0.8
Analyser flags	Blasts +++	

a. Interpret the patient's full blood count results (Table 1). (5%)

b. Propose and justify a differential diagnosis and recommend, with reasons, a series of additional tests that could elucidate a definitive diagnosis. (20%)

c. Figure 1 shows this patient's peripheral blood film. Review the images below and describe the morphological features present (magnification x600). (10%)





The patient is admitted to hospital and a repeat FBC confirms the results. A coagulation screen with D-dimer and Clauss Fibrinogen is performed.

d. Interpret the results in Table 2 and discuss their significance and the underlying pathology (15%)

Table 2: Haemostasis Investigations

Haemostasis		
	Result	**Reference range**
Prothrombin Time	24	11-14s
Activated partial Thromboplastin Time	47	24-34 s
D-dimer ng/mL	9428	0-350
Clauss Fibrinogen g/L	0.9	1.9-4.8

e. A bone marrow aspirate was taken and is pictured below. Describe the morphological features present in the three images below. (10%)

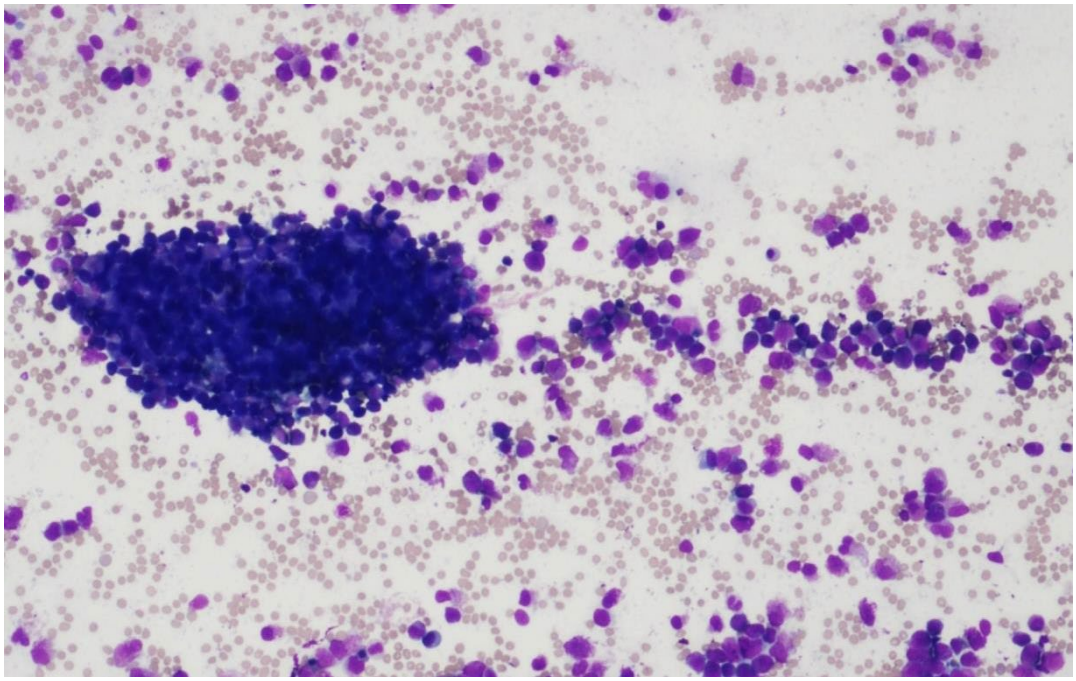


Image 1 (magnification x100)

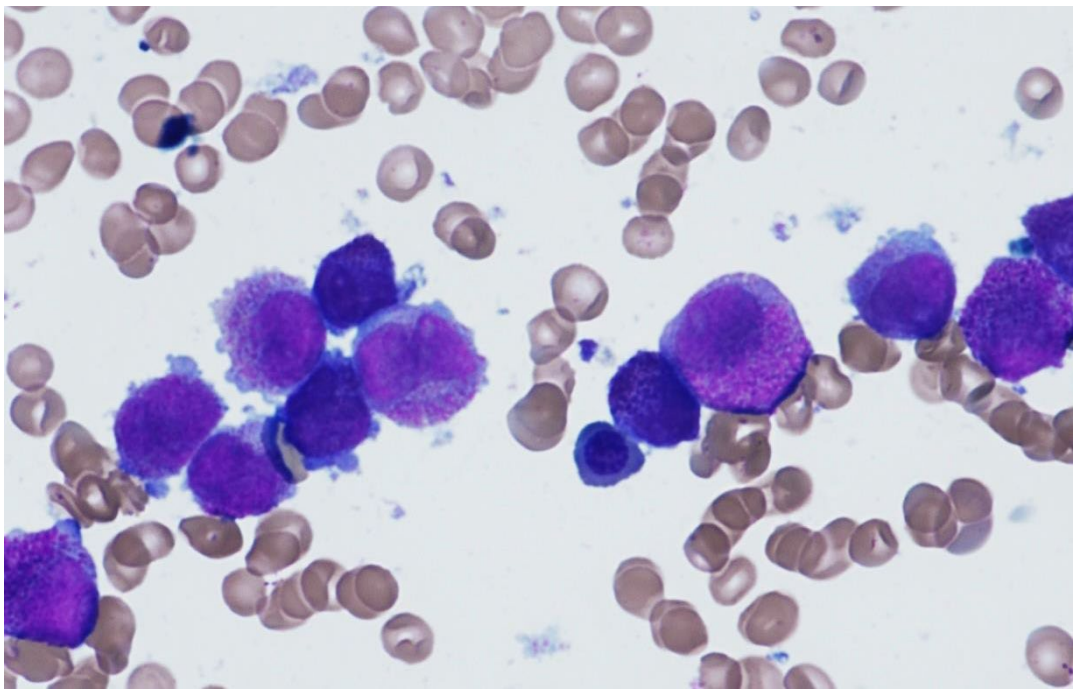


Image 2 (magnification x600)

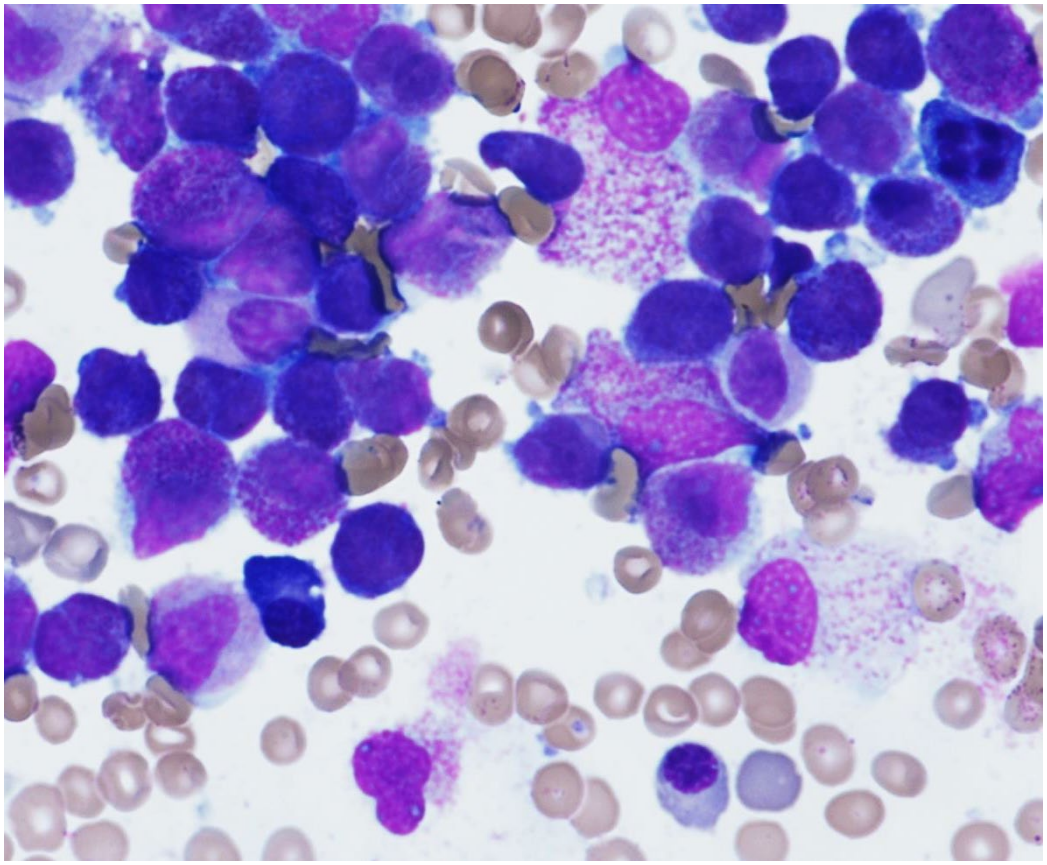


Image 3 (magnification x600)

f. Briefly evaluate the roles of the bone marrow aspirate and trephine for the diagnosis of haematological abnormalities. (15%)

g. Immunophenotyping was performed on this patient and the following results were obtained Table 3. Discuss the results below and the role of Immunophenotyping in the diagnosis of haematological malignancy. (15%)

Table 3: Bone Marrow Immunophenotyping

Marker	**Result**
High SSC	Markedly increased
CD45	100%
CD117	100%
CD33	100% (mod to bright)
CD13	0%
CD34	1%
HLA-DR	0%
CD11b	0%
CD19	0%

Cytogenetics sample was sent to the regional genetics laboratory and 10 metaphase cells were examined by G-band chromosome analysis with the following results.

Karyotype:
45,X,-Y,t(15;17)(q24;q21),add(15)(q25),-22,+mar[9]/
46,XY [1]

h. Discuss these results. Do they confirm your diagnosis? Do they confer a poor prognosis or a favourable prognosis? (10%)

UNSEEN CASE STUDIES

2.
An 68 year old woman presents in A&E with a bruised left knee. The clinician requests a full blood count and coagulation screen. Results are shown in table 1.

Table 1: Initial Investigations

Full Blood Count	**Result**	**Reference Range**
White Blood Cell count ($x10^9$/L)	6.0	4.0-11.0
Haemoglobin (g/L)	122	120-170
Platelets	420	150-450
Red cell count ($x10^{12}$/L)	4.8	4.3-5.7
Haematocrit	0.47	(0.37-0.51)
Mean Cell Volume (fL)	90.4	80-100
Neutrophils ($x10^9$/L)	3.5	2.0-7.0
Lymphocytes ($x10^9$/L)	2.0	1.0-3.0
Monocytes ($x10^9$/L)	0.5	0.2-0.8
Coagulation Screen	**Result**	**Reference Range**
Prothrombin Time	24	11-14s
Activated partial Thromboplastin Time	102	24-34 s
Fibrinogen	2.5	1.5-4.0g/l

a. Comment on these results. (10%)

b. From the information provided, what conclusions can you draw at this stage? (15%)

c. Describe how you would further investigate this patient, explaining your decisions. (20%)

A FVIII assay is performed, using a freshly prepared calibration curve, and the analyser produces the following results on the patient sample.

Sample dilution	Calibrant plasma clotting time	Patient sample clotting time
1/5	50s	75s
1/10	60s	77s
1/20	70s	79s
1/40	80s	82s

d. Comment on these results. (5%)

e. At this stage, which pre-analytical errors could have caused these results? (5%)

The lab decides to perform an inhibitor assay, using the following protocol.
Tube 1: 1:1 mix of diluted patient plasma plus buffered control plasma
Tube 2: 1:1 mix of FVIII deficient plasma plus buffered control plasma
Incubate for 2 hrs and measure residual FVIII activity of tube 1 relative to tube 2.

f. Why are they using this particular approach? (10%)

The following results are obtained.

Sample dilution	Residual Factor VIII level
1/5	15%
1/10	35%
1/20	50%
1/40	72%
1/80	85%

g. Estimate the inhibitor titre from these data. (10%)

h. Comment on the significance of this result. (5%)

The haematologist has requested testing the patient for anti-porcine FVIII inhibitors.

i. Why have they made this request? (5%)

The patient is treated with emicizumab as part of a trial, and one month later the laboratory obtains the following results.

APTT 20s (reference range 24-34s)

1-Stage FVIII assay 450u/dl (reference range 45-165u/dl)

j. Comment on these results. (5%)

k. If the patient had been an 11 month old boy presenting with two month history of swollen knee joints and the same results, would this lead to a different diagnosis? Explain your answer. (10%)

3. A 20-year-old man from Iceland was referred with a history of tiredness, shortness of breath, apparent jaundice, and mild splenomegaly. Laboratory investigations were as follows:

Parameter	Results	Reference range	Units
WBC	5.0	3.7 - 9.5	x 10^9/L
Neutrophils	3.0	1.7 - 6.1	x 10^9/L
Lymphocytes	1.5	1.0 - 3.2	x 10^9/L
Monocytes	0.45	0.2 - 0.6	x 10^9/L
Eosinophils	0.025	0.03 - 0.46	x 10^9/L
Basophils	0.025	0.02 - 0.09	x 10^9/L
RBC	4.0	4.5 - 5.5	x 10^{12}/L
Hb	120	133 - 167	g/L
MCV	80	80 - 98	fL
MCH	*****	27.3 - 32.6	pg
MCHC	*****	316 - 349	g/L
Reticulocytes	200	25 - 125	x 10^9/L
Platelets	210	150 - 400	x 10^9/L
ESR	10	<10	mm/1st hour

Blood film
normocytic, normochromic red cells, polychromasia, spherocytes, schistocytes. Some atypical mononuclear cells.

Bone marrow aspirate
easy tap, hypercellular with a mild erythroid hyperplasia, M/E ratio 1:1

Liver function tests
Bilirubin 33.2 µmol/L (reference range <21). All other LFTs and U&E gave normal results.

a. Calculate the MCH and MCHC values. (5%)

b. Name and comment on the abnormal laboratory results. (5%)

c. Suggest and justify an initial diagnosis. (10%)

d. Explain the value of direct and indirect antiglobulin tests, osmotic fragility testing and red cell survival studies in confirming the diagnosis you have just made. In your answer, describe the methods available for each test, the equipment required, and how any results may modify your initial diagnosis. (10% each test, total 30%)

The antiglobulin tests for this patient were negative, the osmotic fragility test positive, and the red cells showed a markedly shortened lifespan.

e. Comment on the diagnostic value of this new information and use it to confirm, refute or refine your initial diagnosis. Justify your response. (20%)

f. Suggest further tests and comment on how these will help the diagnosis. (20%)

g. Suggest how this patient may be treated clinically. (5%)

h. Would this patient require monitoring of their treatment, and if so how? (5%)