Higher Specialist Diploma

Haematology

Examination – September 2023

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 question on a new page.

4. Each question is worth 25 marks.

1. You are asked to establish a new assay in your laboratory for a direct oral anticoagulant (DOAC). Discuss how you would approach this.

2. You are the BMS reviewing the blood film on a 72-year-old male patient who has recently undergone an emergency laparotomy and hemicolectomy and presents with the following results. Prior to this episode there are no previous results. Comment on the results and explain what further actions you would take.

Parameter	Reference Range	17.04.22	18.04.22	19.04.22
Hb	(120-170 g / L)	101	113	99
WBC	(4.0-11.0 $x10^9$ / L)	32.7	34.0	34.02
PLT	(150-450 $x10^9$ / L)	897	942	614
MCV	(80-100 fL)	97.3	98.5	98.1
Neutrophils	(2.0-7.5 $x10^9$ / L)	25.50	27.54	22.60
Lymphocytes	(1.1-3.6 $x10^9$ / L)	0.65	2.72	3.03
Monocytes	(0.2-0.8 $x10^9$ / L)	0.33	1.36	0.00
Eosinophils	(0.04-0.4 $x10^9$ / L)	0.33	0.68	1.35
Basophils	(0.0-0.1 $x10^9$ / L)	0.00	0.00	0.00
Metamyelocytes		1.31	0.34	0.00
Myelocytes		1.31	1.01	1.52
Promyelocytes		0.00	0.00	0.00
Blast Cells		3.27	3.37	5.52
NRBCs per 100 WBC		2	2	3
CRP	0-5ng / L	172	109	89
Blood film comments from 17.04.2022	Leucoerythroblastic blood film with neutrophilia, left shift, myelocytes approximately 10% blasts with deeply basophilic vacuolated cytoplasm and prominent nucleoli			

3. You are asked by your line manager to prepare a strategy for quality control of your new haematology analyser. Describe the plan you would make for this, justifying your proposals.

4. You have been asked to determine the uncertainty of measurement in your laboratory for blood film and bone marrow aspirate review. Briefly describe the errors you may encounter that can affect the results produced and how you will reduce them.

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Essay Paper

120 minutes

Attempt 2 out of 5 questions

Instructions to candidates

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

3. Begin each new question on a new page.

4. Each question is worth 100 marks.

1. Critically discuss the role the routine haematology laboratory plays in the diagnosis and monitoring of blood-borne tropical infections in the UK.

2. Evaluate the impact of sex-specific definitions of anaemia in modern-day healthcare.

3. Critically evaluate the laboratory investigation of heritable thrombophilia.

4. Critically discuss the role of point of care testing in haemostasis.

5. Using appropriate examples, critically discuss the classification of haematological malignancy and the challenges associated with the classifications systems currently in use.

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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 case study 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

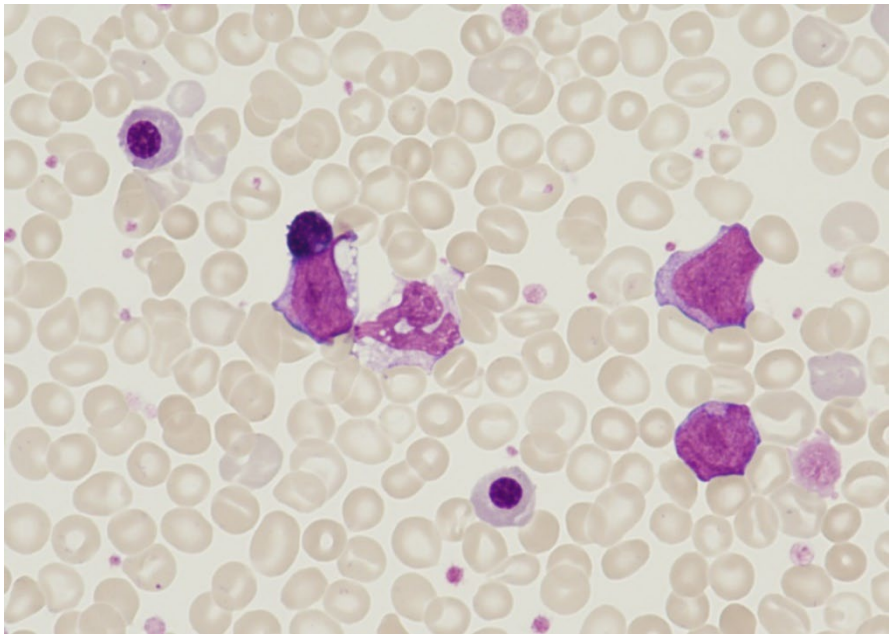
1.

An EDTA specimen is sent routinely to the lab for a full blood count on a neonatal patient born the same day. Clinical details include preterm, suspected sepsis, tetralogy of Fallot and duodenal atresia. The Advia 2120 analyser results are below:

Parameter	Result	Reference Range	Units
White Blood Cell Count	44.5	10.0 - 26.0	$x10^9$ / L
Haemoglobin	146	145 - 220	g / L
Platelets	287	150 - 450	$x10^9$ / L
Red cell count	3.61	3.9 – 5.5	$x10^{12}$ / L
Mean Cell Volume	131.3	95 - 125	fL
Neutrophils	7.3	2.9 - 14.5	$x10^9$ / L
Lymphocytes	10.0	2.0 - 11.0	$x10^9$ / L
Monocytes	1.3	0.0 - 1.9	$x10^9$ / L
Eosinophils	0.1	0.0 - 0.8	$x10^9$ / L
Basophils	0.1	0.0 - 0.1	$x10^9$ / L
Large unstained cells	25.7		

a. Examine the patient's full blood count results and identify the abnormal features. Indicate possible causes for the findings you have identified. Justify your answer.
(10 marks)

Based upon these results, a blood film was produced and evaluated. An image from this film is shown below:



b. Comment on the morphology present. What is your differential diagnosis and what further actions would you take? (10 marks)

You perform a manual differential on the blood film and obtain the following results:

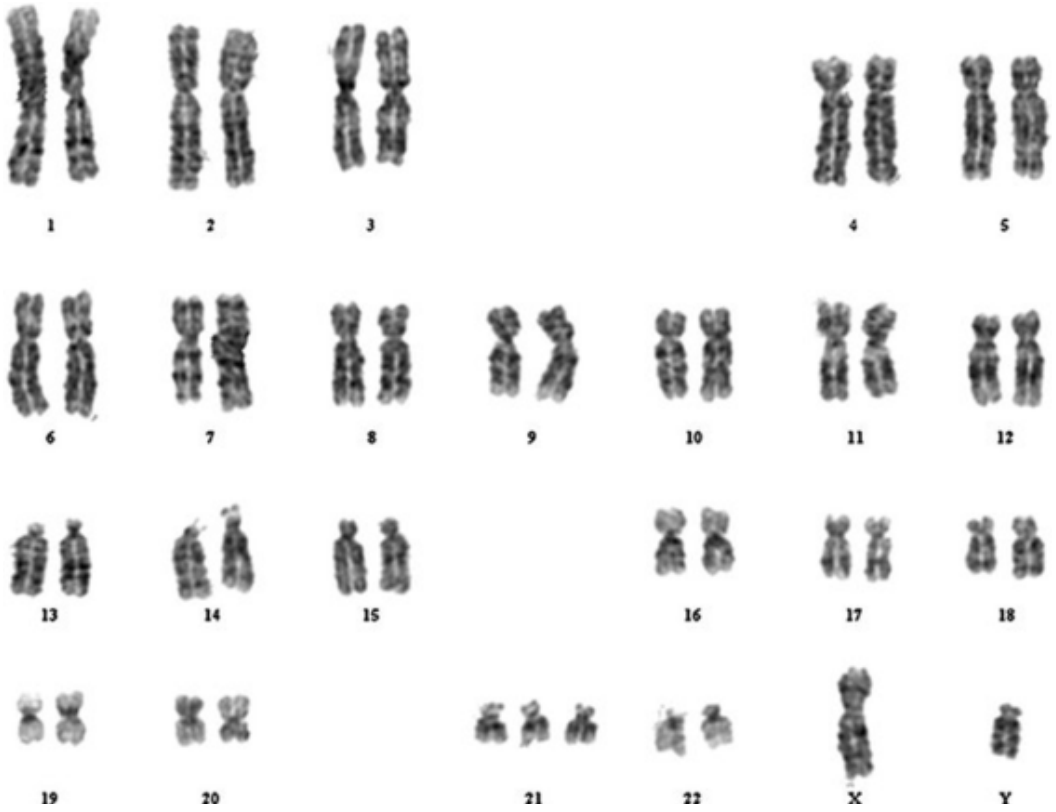
Parameter	Result	Reference Range	Units
Analyser WBC	44.5	10.0 - 26.0	$x10^9$ / L
Manual Differential			
Neutrophils	3.71	2.9 - 14.5	$x10^9$ / L
Lymphocytes	1.43	2.0 - 11.0	$x10^9$ / L
Monocytes	0.57	0.0 - 1.9	$x10^9$ / L
Eosinophils	0.0	0.0 - 0.8	$x10^9$ / L
Basophils	0.0	0.0 - 0.1	$x10^9$ / L
Metamyelocytes	0.28		
Myelocytes	1.14		
Promyelocytes	0.00		
Blasts	21.39		
NRBCs per 100 WBC	56		

c. Correct the WBC for the presence of nucleated red blood cells and determine the percentages of the white cells present. Discuss the WBC differential results and the differential diagnosis. (5 marks)

You phone and speak to the nurse looking after the neonate and ask them if there are any further clinical details. She tells you the baby has presented with a complex clinical picture but has poor muscle tone, a flat nasal bridge and mid-face, and the clinical team suspect a genetic abnormality.

d. Does this information change your suspected diagnosis? What is the suspected genetic abnormality and describe the physical traits and clinical findings often associated with this abnormality? (10 marks)

Samples are sent for chromosomal analysis and the following karyotype is produced:



e. Comment on the karyotype above and the relevance of this finding. How does this abnormality occur? (10 marks)

f. Further cytogenetic analysis confirms an acquired mutation in GATA1. What is the role of GATA1 in normal haematopoiesis? (10 marks)

g. What is your suspected diagnosis? What is the clinical presentation? (10 marks)

h. Provide an overview of the pathogenesis of your suspected diagnosis. (25 marks)

i. The patient has a follow-up FBC at 3 months of age which is normal. What is the prognosis for the patient? And what further steps should be taken for this patient? (10 marks)

UNSEEN CASE STUDIES

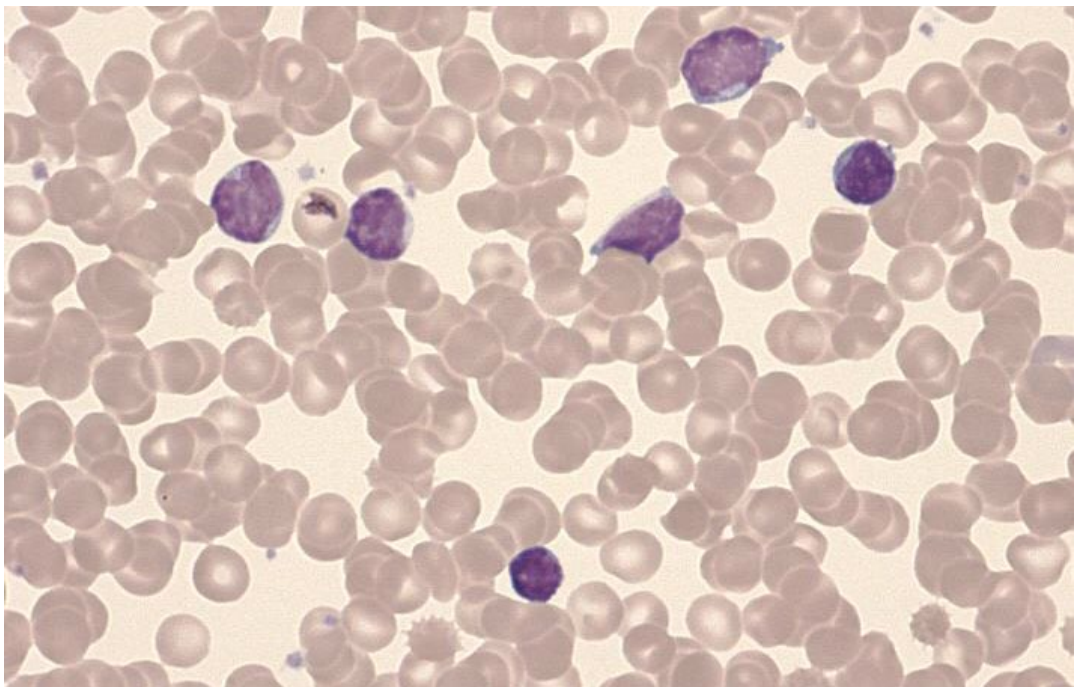
2.

An EDTA specimen is sent to the lab for a full blood count on a 53-year-old female GP patient for routine monitoring. The analyser results are below:

Parameter	Result	Reference Range	Units
White Blood Cell Count	14.3	4.0-11.0	$x10^9$ / L
Haemoglobin	131	115-165	g / L
Platelets	280	150-450	$x10^9$ / L
Red cell count	4.22	3.80-5.50	$x10^{12}$ / L
Mean Cell Volume	95.3	80-100	fL
Neutrophils	3.5	2.0-7.5	$x10^9$ / L
Lymphocytes	9.7	1.5-4.0	$x10^9$ / L
Monocytes	0.9	0.2-0.8	$x10^9$ / L
Eosinophils	0.2	0.04-0.40	$x10^9$ / L
Basophils	0.0	0.0-0.1	$x10^9$ / L

a. Examine the patient's full blood count results and identify the abnormal features. Indicate possible causes for the findings you have identified. Justify your answer.
(5 marks)

Based upon these results, a blood smear was produced and evaluated. An image from this smear is shown below:



b. Identify the white cell features above. What is your differential diagnosis and what further actions would you take? (5 marks)

The patient attends the haematology clinic and immunophenotyping and cytogenetics are performed. The immunophenotyping shows:

63% cells belong to a neoplastic population with the following phenotype:

Positive for: CD5 CD19 CD23 CD200 and lambda
Negative for: CD10 CD79b CD38 CD103

c. Does this confirm your suspected diagnosis? What would this phenotype be consistent with? Justify your answer. (10 marks)

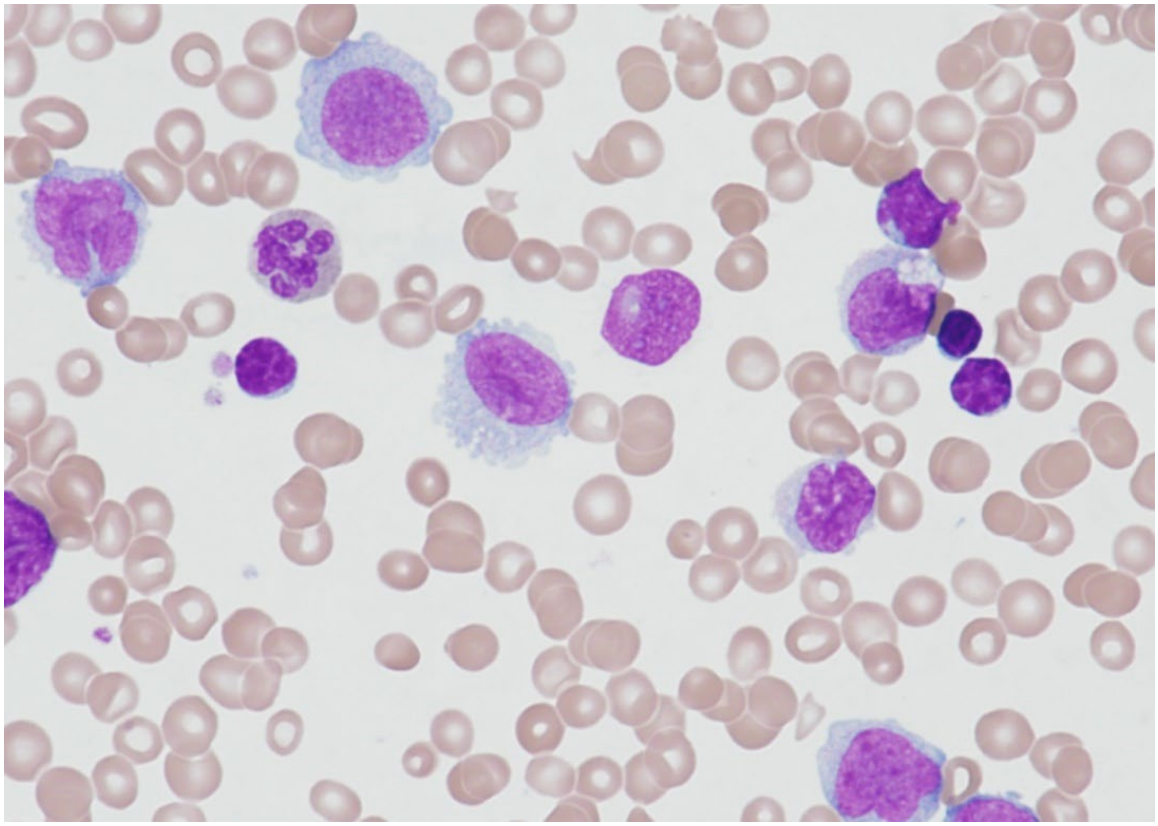
The patient is put on a watchful wait protocol but 3 weeks later she phones her clinical nurse specialist stating that she 'feels very unwell'. A follow-up FBC and blood film is performed with the following results:

Parameter	**Result**	**Reference Range**	**Units**
White Blood Cell Count	29.9	4.0-11.0	$x10^9$ / L
Haemoglobin	108	115-165	g / L
Platelets	195	150-450	$x10^9$ / L
Mean Cell Volume	103.8	80-100	fL
Neutrophils	11.06	2.0-7.5	$x10^9$ / L
Lymphocytes	8.67	1.5-4.0	$x10^9$ / L
Monocytes	3.08	0.2-0.8	$x10^9$ / L
Eosinophils	0	0.04-0.40	$x10^9$ / L
Basophils	0	0.0-0.1	$x10^9$ / L
Metamyelocytes	0		
Myelocytes	0.6		
Promyelocytes	0		
Blasts	6.49		
CRP	13.7	0-5	Ng / mL

d. Comment on the above findings. What is your suspected diagnosis? (10 marks)

The image below is taken from the blood film on the follow-up FBC:

(see next page for image)



e. Comment on the morphology present and your suspected diagnosis. What further investigations would be useful? Justify your answer. (10 marks)

Follow-up immunophenotyping on bone marrow showed the following 29% neoplastic B cells CD5+ CD19+ CD23+ lambda+ CD200 + Immunophenotyping confirms the presence of MDS / MPN – CMML.

f. What additional markers would you have tested to reach this diagnosis and why? (10 marks)

The bone marrow aspirate and trephine at this point confirm 15% monoblast / promonocytes.

g. Explain how this would be classified using the WHO classification of Haematolymphoid Tumours 2022 Revision 5, giving an overview of the WHO CMML classification from this edition. (15 marks)

Initial cytogenetic analysis was performed at the time of the CLL diagnosis and showed TP53 deletion, ATM not deleted, IGHV unmutated.

h. Discuss the significance of these findings. (10 marks)

Further cytogenetic analysis was performed when the patient developed a monocytosis and an increase in blasts. Cytogenetics showed a NPM1 mutation and a FLT3-ITD mutation.

i. Do these mutations fit with your suspected additional diagnosis? What are the prognostic implications of the cytogenetic abnormalities discovered in this patient and how can their presence affect treatment decisions? Justify your answer. (15 marks)

j. What is your final diagnosis? Does the presence of any of the cytogenetic abnormalities change your diagnosis? Justify your answer. (10 marks)

3.
A 25-year-old man with a reported history of easy bruising and epistaxis has been referred to the haematology clinic for investigation.

a. What information would you expect the clinician to request. Explain the significance of the information? (15 marks)

b. Clinician has asked for a bleeding time to be performed. How would you respond? (5 marks)

Initial laboratory results have revealed the following:

Parameter	**Result and units**	**Reference range**
WBC	5.7 x 10^9/L	4.0–11.0
Hb	125 g/L	120–160
Platelets	200 x 10^9/L	150–400

PT	12 sec	10 – 13
APTT	40 sec	30 – 40
Fibrinogen	2.5g/L	2.0 – 4.0

FVIII:C	40 iu/dL	50 – 150
FIX:C	89 iu/dL	50 – 150
FXI:C	121 iu/dL	50 – 150
FXII:C	82 u/dL	50 – 150

VWF:Ag	35 iu/dL	50 – 150
VWF Activity	15 iu/dL	50 – 150
VWF:CB	18 iu/dL	50 – 150

c. Comment on these results. (15 marks)

d. Which (if any) preanalytical variables may have influenced these results? (5 marks)

e. The reference ranges reported for factor assays and VWF assays are obtained from the manufacturer's data insert. What pitfalls are associated with this approach? What influence will the reference ranges have on your diagnosis. (10 marks)

f. Is the above report sufficiently detailed with respect to the VWF results? If not, what further information should be reported with respect to the VWF activity assay and why? (10 marks)

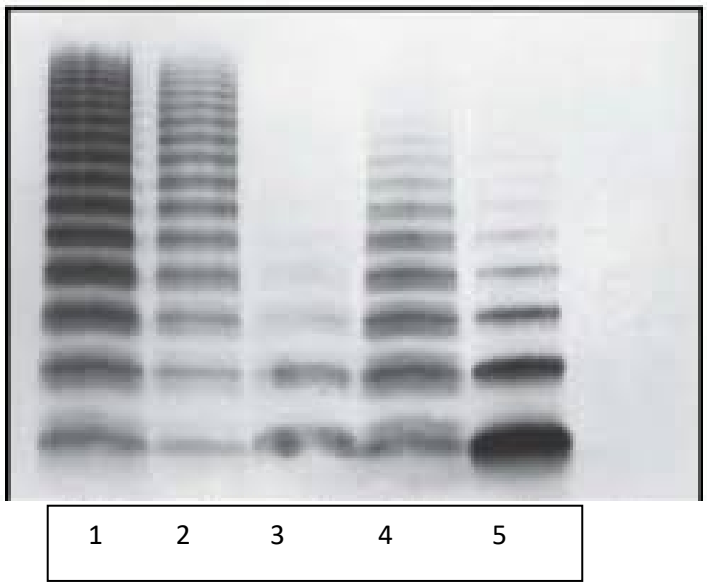
g. A request has been made to obtain a blood group for this patient? Why may this have been requested? Would it assist the diagnosis? Justify your answer. (5 marks)

The clinician also requested Platelet Function Analyser and Platelet aggregometry tests on this patient. Results were:
PFA - CEPI (collagen / epinephrine) : Result >250s, reference range 78-199s
CADP (collagen / epinephrine) : Result >200s, reference range 55-137s
Platelet aggregation – reduced aggregation with all agonists (collagen, epinephrine, APD, ristocetin).

h. Comment on these findings. (10 marks)

i. What other investigations would be useful to confirm your diagnosis? (10 marks)

j. VWF multimer analysis is shown below. Comment on these results. Lane 1 is a normal control and this patient's sample was run in lane 5. (10 marks)



k. From your diagnosis, what treatment options are recommended for this patient? (5 marks)