Higher Specialist Diploma

Haematology

Examination 2018

Paper 3

Discipline-specific questions

120 minutes

Attempt 3 out of 6 questions

Instructions to candidates

1. Record your candidate number, qualification title and where appropriate the discipline and examination paper number on the front sheet of the answer booklet
2. Record your candidate number and the page number in the spaces provided on the answer sheets
3. Begin each new answer on a new page
4. Write on one side of the answer sheet only
5. Each question is worth 100 marks

1. Discuss the effects of storage on haematological analyses.

2. Critically discuss techniques available to investigate haemoglobinopathies caused by defects in the globin genes.

3. Evaluate the contribution of the laboratory to a diagnosis of cobalamin and folate deficiency.

4. Critically discuss the causes of eosinophilia and the laboratory procedures used for the investigation of this condition.

5. Critically evaluate the generation and application of reference ranges and cut-off values in the diagnosis of haemostatic disorders.

6. Critically evaluate the activated partial thromboplastin time as a tool for screening, diagnosis and treatment monitoring of disorders of haemostasis and thrombosis.

Higher Specialist Diploma

Haematology

Examination 2018

Paper 4

Case studies

120 minutes

Attempt all case studies

Instructions to candidates

1. Record your candidate number, qualification title and where appropriate the discipline and examination paper number on the front sheet of the answer booklet
2. Record your candidate number and the page number in the spaces provided on the answer sheets
3. Begin each new answer on a new page
4. Write on one side of the answer sheet only
5. **Each case study is worth 100 marks**

Seen case study

1.

A 10 year old Caucasian female was investigated for a one year history of recurrent jaundice associated with dark urine and pale stools. Her past history was non-contributory.

Slight jaundice was present at the time, the tip of the spleen was palpable but there was no lymphadenopathy or hepatomegaly. Bone marrow showed a normoblastic hyperplasia. Her full blood count results are shown in Table 1.

Table 1: Results from the initial full blood count investigation

Parameter	Result	Reference range	Units
Haemoglobin	108	133 - 167	g/L
Haematocrit	0.33	0.37 – 0.47	L/L
Mean Cell Volume	95	80 - 99	fL
Reticulocytes	210	50 - 100	x 10^9/L
Platelets	255	150 - 400	x 10^9/L
White Blood Cell Count	8.0	4.0 - 10.0	x 10^9/L
Neutrophils	5.2	2.0 - 7.0	x 10^9/L
Lymphocytes	1.9	1.0 - 3.0	x 10^9/L
Monocytes	0.8	0.2 - 1.0	x 10^9/L
Eosinophils	0.07	0.02 - 0.5	x 10^9/L
Basophils	0.03	0.02 - 0.1	x 10^9/L
RBC morphology	Anisocytosis ++ Polychromasia ++	Poikilocytosis + Ovalocytosis +	Echinocytes +

a. Comment on the above clinical and laboratory data. (10%)

The results of subsequent investigations are shown in Table 2.

Table 2: Follow-up investigations

Parameter	Result	Reference range	Units
Total bilirubin	51	<17	µmol/L
Conjugated bilirubin	4.0	<5.2	µmol/L
ALT	21	5 - 42	IU/L
AST	34	10 - 50	IU/L
Serum iron	7.1	0.6 – 2.0	mg/L
Ferritin	278	10 - 200	µg/L
Haptoglobin	0.4	0.8 – 2.7	g/L
Osmotic fragility	Normal		
Hb HPLC	Normal		
Direct antiglobulin test	Negative		

b. Based on all data available up to this point, make and justify a preliminary diagnosis. (10%)

A panel of red cell component assays was then performed. The results are given in Table 3.

Table 3: Red Cell Component Assays

Parameter	Result	Reference range	Units
G6PD	18.9	8.8 – 13.4	U/g Hb
Pyruvate kinase	5.2	9.0 – 22.0	U/g Hb
Pyruvate kinase (low substrate)	1.6	1.0 – 2.6	U/g Hb
Glucose phosphate isomerase	84	38 - 83	U/g Hb
Phosphofructokinase	11.1	6.3 – 15.7	U/g Hb
Phosphoglycerate kinase	342	195 - 340	U/g Hb
Aldolase	3.3	1.4 – 5.0	U/g Hb
Hexokinase	6.8	1.0 – 2.5	U/g Hb
2,3-diphosphoglycerate	38.7	10.5 – 16.5	µmol/g Hb
Pyrimidine 5' nucleotidase screen	Normal		

c. Make a diagnosis and discuss the red cell component assay results in light of the other data, relating then to the pathophysiology of the disorder. **(20%)**

d. Describe the principle of, and critically evaluate, pyruvate kinase activity assays. **(20%)**

e. Why do patients with this disorder tend to tolerate low haemoglobin levels? **(10%)**

DNA analysis of the *PK-LR* gene revealed a cDNA 1529 G>A (Arg510Gln) missense mutation and a cDNA 694 G>T (Gly232Cys) missense mutation.

f. Comment on these findings. **(5%)**

g. In what clinical situation might a patient with this disorder undergo splenectomy and what effects would it have on their haematology? **(10%)**

h. In what ways does this disorder modulate infection with malaria? **(10%)**

i. How would co-inheritance with Gilbert's syndrome affect the laboratory presentation? **(5%)**

Unseen Case Studies

2.
A 2 year old male is referred to A&E because of a swollen knee. Investigation reveals a bleed into the joint. Initial laboratory results are shown in Table 2.1.

Table 2.1 Initial laboratory results

Parameter	Result	Reference range	Units
WBC	5.7	4.0 – 11.0	x 10^9/L
Hb	120	120 – 160	g/L
Platelets	350	150 – 400	x 10^9/L
PT	12	10 – 13	Sec
APTT	90	30 – 40	Sec
Fibrinogen	2.5	2.0 - 4.0	g/L

a. Comment on these results. (10%)

b. What is the most likely cause of the bleeding in this child? Justify your answer. (15%)

c. Suggest some other possible causes of this result. (10%)

d. What clinical and family information would be helpful in this investigation? (10%)

Further laboratory results were obtained and are shown in Table 2.2.

Table 2.2 Follow-up assays

1-stage clotting assays	Result	Reference range	Units
FVIII:C	50	50 – 150	iu/dL
FIX:C	89	50 – 150	iu/dL
FXI:C	121	50 – 150	iu/dL
FXII:C	82	50 – 150	u/dL
VWF parameters			
VWF:Ag	100	50 – 150	iu/dL
VWF Activity	110	50 – 150	iu/dL
VWF:CB	105	50 – 150	iu/dL

e. Comment on the results from Table 2.2. (10%)

A further sample was obtained from this child, and sent to a referral centre – the results in Table 2.3 were returned from this centre.

Table 2.3 Results from referral centre

Factor assays	**Result**	**Reference range**	**Units**
FVIII:C chromogenic assay	10	50 – 150	iu/dL
1-stage clotting assays			
FIX:C	100	50 – 150	iu/dL
FXI:C	111	50 – 150	iu/dL
FXII:C	99	50 – 150	u/dL
VWF parameters			
VWF:Ag	80	50 – 150	iu/dL
VWF Activity	90	50 – 150	iu/dL
VWF:CB	80	50 – 150	iu/dL

f. Comment on the results from Table 2.3. What conclusions and/or diagnosis can you make? (10%)

g. Why might you get a discrepant 1-stage and chromogenic assay result when investigating a possible diagnosis of haemophilia? (5%)

An unrelated adult also arrives in A&E with a bleed into their joints. This patient is known to have severe haemophilia A, and they are on prophylactic FVIII treatment. They inform you their last infusion was one hour ago. Your laboratory measures the FVIII level with your 1-stage assay – the result is 30iu/dL.

h. Comment on this result – is this the level of FVIII you might expect in a post-infusion sample? (10%)

i. If a chromogenic FVIII assay was performed and gave a level of 60IU/dL, what conclusions could you draw? What information would you want from the clinicians or patient? **(10%)**

j. If a chromogenic FVIII assay was performed and also gave a level of 30IU/dL, what conclusions could you draw? What further tests would you recommend, and what treatment options may be available for this patient? (10%)

3.
A 51 year old male reported to his general practitioner complaining of bleeding gums for the last three months and unintentional weight loss of 5Kg over the last six months. His previous dental appointment nine months ago had been unremarkable.

The patient's physical examination revealed that he was moderately built, poorly nourished and pale. Oral examination revealed generalised soft, oedematous gingival enlargement accompanied by sublingual ecchymoses. A full blood count was requested with the results presented in Table 3.1.

Table 3.1: Results from the initial full blood count investigation

Parameter	Result	Reference	Units
Red cell count	2.11	4.3 - 5.7	x 10^{12}/L
Haemoglobin	56	133 - 167	g/L
Mean Cell Volume	82	77 - 98	fL
Mean Cell Haemoglobin	26.5	26 - 33	pg
Platelets	25	143 - 400	x 10^{9}/L
White Cell Count	112	4.0 - 10.0	x 10^{9}/L
Neutrophils	12.1	2.0 - 7.0	x 10^{9}/L
Lymphocytes	3.6	1.0 - 3.0	x 10^{9}/L
Monocytes	25.8	0.2 - 1.0	x 10^{9}/L
Eosinophils	0.5	0.02 - 0.5	x 10^{9}/L
Basophils	0.1	0.02 - 0.1	x 10^{9}/L
Blasts/atypical cells	69.9	<0.1	x 10^{9}/L

a. Referring to the data included in table 1, explain the initial haematology results. (20%)

An extended differential count of the peripheral blood cells to elucidate the identity of the atypical cells revealed the results shown in Table 3.2.

Table 3.2: Extended differential count

Cell population	Percentage	Absolute (x 10^{9}/L)
Myeloblasts	***	28
Monoblasts	***	16.8
Promonocytes	***	24.64
Promyelocytes	***	0.112
Myelocytes	***	0.112
Metamyelocytes and band forms	***	0.224

b. Calculate the percentages for each of the populations included in table 2 and provide an interpretation of these results. (20%)

Subsequently, a Romanowsky stained peripheral blood film was examined. An example of noteworthy cells is provided in figure 1.

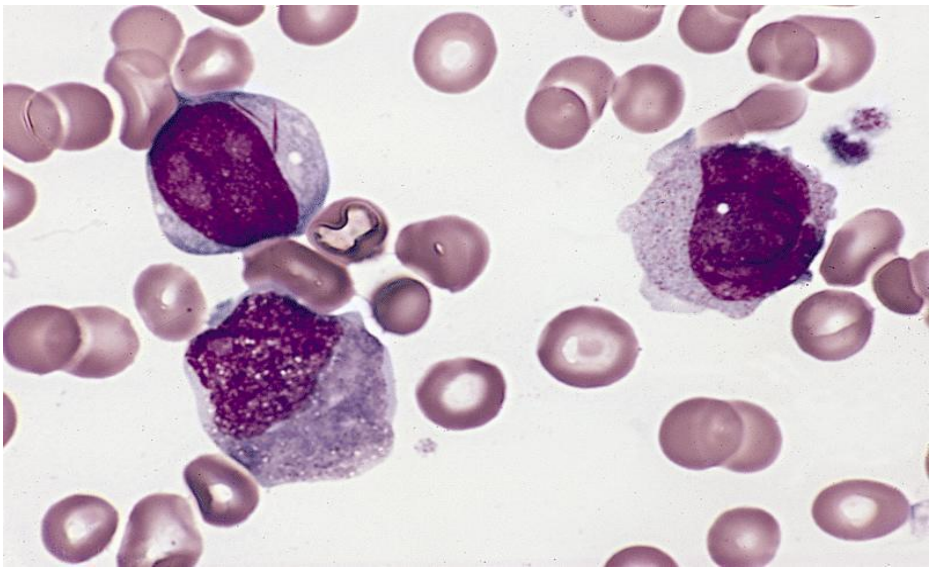

Figure 1: Peripheral blood film requested from the initial full blood count specimen.

c. Examine the photomicrograph presented in figure 1. Considering the morphological characteristics of each, identify the white cells represented in this figure and comment on their contribution to the patient's condition. (30%)

Amongst the further investigations, immunophenotyping and cytochemistry data were collected. The results of these investigations are shown in Table 3.3.

Table 3.3 Immunophenotyping and cytochemistry data obtained following initial investigations.

	Immunophenotype										**Cytochemistry**	
Population 1	CD45 +	CD13 +	CD33 +	CD34 +	CD117 +	HLA-DR +	-	-	-	-	MPO + (5%)	-
Population 2	CD45 +	CD13 +	CD33 +	-	-	HLA-DR +	CD11b +	CD11c +	CD15 +	CD64 +	-	NSE +

Key: MPO = Myeloperoxidate; NSE = Non-specific Esterase

d. For each population comment on the markers and identify the cells presented in the table above. (20%)

e. Briefly explain how this condition is classified according to the World Health Organisation. (10%)