HAEMBASE

Mock FRCPath Part 2 Morphology Paper November 2022

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SUGGESTED ANSWERS

Answers are based on the real film reports (+/- other pathology reports) for each case. Answers for questions about further investigation / management are purely based on my own thoughts – you may have other equally legitimate answers. This is for practice, not definitive exam truth!

Question 1. A 25-year-old woman presents to her GP with two weeks of breathlessness, chest pain and tachycardia on walking. She has no past medical history. Her only medication is the combined oral contraceptive pill.

Hb 49, WBC 3.8, Plt 355, Neut 2.3

a. Report the blood film (3 marks)

Normal platelets
Red cell anisocytosis, macrocytosis, ovalcytes, tear drop poikilocytes
Hyperlobated neutrophils

b. State your preferred diagnosis, or a short differential (1 mark)

Megaloblastic anaemia. This case is combined B12 and folate deficiency
B12 100 ng/l, Folate <3.0 ug/l, Ferritin 350

c. List three further tests you would request (3 marks)

Folate
Vitamin B12 / Serum cobalamin / Plasma Methylmelonic Acid / Plasma total homocystein
Reticulocyte count
Ferritin
Intrinsic factor antibodies / Gastric parietal cell antibodies
Coeliac screen

Question 2. An 80-year-old woman presented to the emergency department with five days of fever and lethargy.

Hb 105, WBC 53, Plt 43, Cr 184

a. Briefly report the bone marrow aspirate (3 marks)

Hypercellular bone marrow aspirate showing 90% blasts (medium to large cells with NC ratio and some with prominent nucleoli). Marked reduction in normal haematopoiesis. Appearances consistent with a diagnosis of acute leukaemia / acute myeloid leukaemia.

(N.B. this photo also shows cells in several stages of mitosis, reflecting the high proliferation rate in acute leukaemia)

b. Immunophentyping (flow cytometry) is performed. On the basis of this phenotype, state the one additional test that is most urgently required (1 mark)

CD13+, CD33+, CD64+, CD117+, MPO+
CD34-, HLADR-, CD2-, CD19-

FISH for PML-RARA (t(15;17)). Absence of CD34 and HLA-DR is associated with APML and this needs urgently excluding due to its specific management.

c. Give one example each of a favourable, intermediate and adverse risk genetic abnormality seen in acute myeloid leukaemia (3 marks)

European Leukaemia Network risk stratification 2022:

Risk Category	Genetic Abnormality
Favourable	t(8;21)/RUNX1::RUNX1T1 Inv16/CBFB::MYH11 Mutated NPM1 **without** FLT3-ITD CEBPA mutation (bZIP in-frame)
Intermediate	Mutated NPM1 **with** FLT3-ITD Wild type NPM1 **with** FLT3-ITD t(9;11)/MLLT3::KMT2A Cytogenetic/Molecular abnormalities not classified as favourable or adverse
Adverse	T(6;9)/DEK::NUP214 T(v;11)/KMT2A-rearranged T(9;22)/BCR::ABL1 T(8;16)/KAT6A::CREBBP Inv(3)/GATA2, MECOM(EVI1) T(3;v)/MECOM(EVI1)-rearranged -5 or del(5q), -7, -17/abn(17p) Complex karyotype Monosomal karyotype Mutated ASXL1, BCOR, EZH2, RUNX1, SF3B1, SRSF2, STAG2, U2AF1, ZRSR2 Mutated TP53

Question 3. A 70-year-old woman presents to her GP with 3 months of progressive lethargy and loss of appetite. On examination there is massive splenomegaly. No palpable lymphadenopathy.

Hb 107, WBC 43, Plt 91

a. Report the blood film (3 marks)

Thrombocytopenia
Occasional red cell tear drop poikilocytes
Hyperlobated neutrophils
Leukocytosis of small to medium sized lymphoid cells with notched/clefted nuclei

b. Briefly report the bone marrow aspirate (3 marks)

Hypercellular particles
Trilineage haematoiesis present
Majority of cells seen are small lymphoid cells, many with indented/cleaved nuclei. Some with a faint nucleoli.

(N.B. difficult or impossible to appreciate from a single photo but this patient also had megaloblastic erythroid and granulocytic changes present. Knowing this you may see that the myelocytes in photo above are larger than normally expected.

Flow cytometry in this case:
CD19+, CD5+, CD20+, CD22+, CD79b+, CD81+
CD10-, CD23-, CD38-. CD200-)

c. State your preferred diagnosis along with any relevant differentials (2 marks)

This is a case of mantle cell lymphoma with co-existing folate deficiency
Other low grade lymphomas would be appropriate differentials

Question 4. A two-year-old boy presents to the emergency department for the third time with a limp and right hip pain.

Hb 108, WBC 145

a. Report the blood film (3 marks)

Thrombocytopenia
Red cell rouleaux
Neutropenia
Leukocytosis of blasts – small mononuclear cells with very high NC ratio, some with prominent nucleoli.

b. Immunophenotyping (flow cytometry) of the peripheral blood is performed. What is the diagnosis? (2 marks)

CD19+, CD79a+, CD22+
MPO-, CD2-, CD10-, surface Ig-

This is Pro-B Acute Lymphoblastic Leukaemia

c. Give one reason dexamethasone is preferred to prednisolone in this condition (1 mark)

Greater CNS penetration → reduced CNS relapse rate (RR 0.5)
Better in vitro anti-leukaemic effect
Reduced risk of death, relapse and secondary malignancies
(N.B. Cons = 7x increased rate of myopathy, more neuro SE's, more mid-treatment mortality)

Ref: Dexamethasone versus prednisolone for induction therapy in childhood acute lymphoblastic leukaemia: a systemic review and meta-analysis, O Teuffel, Leukaemia 2011

Question 5. A 55-year-old man is seen in the haematology clinic with an eight-week history of headache and visual blurring. Examination revealed right sided retinal haemorrhage and palpable splenomegaly.

Hb 110, WBC 200, Plt 400

a. Report the blood film (3 marks)

Normal platelets
Red cell rouleaux, nucleated red cells present
Left shifted myeloid leukocytosis. Roughly 50:50 neutrophil:myelocyte split. Basophils present.
Occasional blasts present (<1%)

b. Briefly report the bone marrow aspirate, along with your preferred diagnosis (4 marks)

Hypercellular particles
Megakaryocytes not shown in this picture
Expanded, left shifted granulopoiesis with eosinophilic precursors and occasional blasts.
Reduced erythropoiesis

Conclusion: Appearances consistent with a diagnosis of chronic myeloid leukaemia in chronic phase.

c. Asciminib is approved in the UK as 3rd line therapy in patients with this condition. What is the mechanism of action for asciminib? (2 marks)

BCR-ABL1 inhibitor (Specifically Targeting the ABL Myristoyl Pocket (STAMP))

Question 6. An 80-year-old man is under haematology review for a recent finding of leukocytosis with neutropenia. On examination he has raised, red skin nodules present on his head, face and upper chest.

Hb 74, WBC 35, Plt 97

a. Report the blood film (3 marks)

Thrombocytopenia
Red cell anisocytosis, anaemia, occasional spherocytes
Neutropenia
Medium to large, abnormal mononuclear cells with high NC ratio and prominent nucleoli.

b. Immunophenotyping (flow cytometry) of the peripheral blood is performed. What is the diagnosis? (1 mark)

CD123+, CD4+, CD56+, CD33+
CD34-, CD2-, CD3-, CD13-, MPO-

This is blastic plasmacytoid dendritic cell neoplasm (BPDCN). A typical phenotype for this is CD123+, CD4+, CD56+ ("123456") with negative myeloid and T-cell markers.

c. Briefly state the normal healthy function of the cell of origin in this disorder (2 marks)

Plasmacytoid dendritic cells produce cytokines, particularly type 1 interferon, in response to viral infections → T-cell activation.

Question 7. A 70-year-old woman known to haematology clinic presents to the emergency department with lethargy and breathlessness.

Hb 50, WBC 150, Plt 175

a. Report the blood film (3 marks)

Normal platelets
Red cell anisocytosis with macrocytes, polychromasia, spherocytes and nucleated red cells
Lymphocytosis of small, mature lymphoid cells with condensed nuclear chromatin

b. State your preferred diagnosis (2 marks)

This is a case of autoimmune haemolysis secondary to chronic lymphocytic leukaemia.

c. Briefly outline the principle of performing a direct antiglobulin test (Coombs) (3 marks)

A serological test to detect red cells coated with immunoglobulin/complement

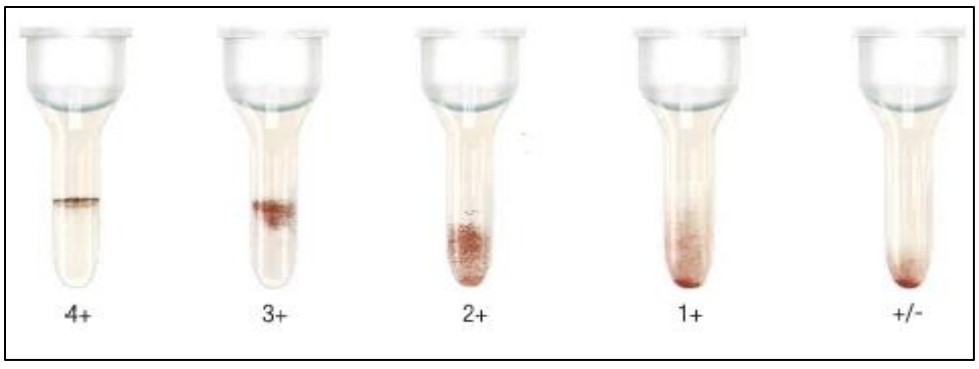
Take whole blood into EDTA
Centrifuge +/- wash to remove plasma and acquire concentrated red cells for testing

E.g. using gel column agglutination:
Patient red cells mixed with anti-human globulin in cartidge wells
Centrifuge

- ➔ Red cells bound by the test globulin will agglutinate and only partially pass through the gel, or not at all (positive result)
- ➔ Red cells not bound by the test globulin will pass through the gel to the bottom of the tube (negative)

If this screening test is positive → repeat with more specific reagents, e.g. Anti-IgG / Anti-C3d

N.B. drawing a picture might save you time writing this all out.



Question 8. A 35-year-old man attends his GP with right upper quadrant pain. He is usually fit and well. He reports a healthy, mixed diet and no symptoms to suggest blood loss. A full blood count is performed.

Hb 109, MCV 72, MCH 25, WBC 6.3, Plt 518

a. Report the blood film (3 marks)

Normal platelets
Marked red cell anisopoikilocytosis, particularly elliptocytes and contracted cells.
Microcytes, mild polychromasia.
Normal lymphocytes. Neutrophils not present in this photo.

b. What test(s) would you perform next to investigate the red cell changes? (2 marks)

Iron studies / ferritin
Haemoglobin electrophoresis / HPLC
(SDS-PAGE for membranopathy (unnecessary if there is an appropriate history and family history))
(Genetic testing)

c. Provide your preferred diagnosis, or differential diagnosis (3 marks)

This case underwent Hb electrophoresis and genetic testing that identified three red cell abnormalities:
- Hereditary elliptocytosis
- Sickle cell trait (HbS 29% on HPLC)
- Alpha+ trait

I think the HE should be obvious and definitely included in answer. It should also be clear that it is not the only abnormality present due to the anisocytosis and contracted cells of non-elliptocytes, so an additional haemoglobinopathy differential should be included.

Question 9. A 35-year-old woman attends the haematology clinic for routine follow-up. Since her last appointment she has been seen in audiology and fitted with bilateral hearing aids. She is also under regular review in the nephrology clinic. Her mother is similarly affected.

a. Report the blood film (3 marks)

Thrombocytopenia with giant platelets
Normal red cells
Neutrophils contain blue inclusion bodies

b. State your preferred diagnosis (2 marks)

Inherited platelet disorder (May Hegglin anomaly / MYH9-related disorder)

c. List three cause of macrothrombocytopenia (3 marks)

Inherited
Bernard-Soulier Syndrome
Grey Platelet Syndrome
Platelet-Type Pseudo VWD
GATA1 Syndrome
Velocardiofacial Syndrome
Paris-Trousseau-Jacobsen Syndrome
(Do you know any I have missed?)

Acquired
Immune thrombocytopenia
Myeloproliferative neoplasms

Question 10. A 10-year-old boy, who recently arrived in the UK from Democratic Republic of Congo, presents to the emergency department with fever, headache, joint pains and cervical lymphadenopathy.

a. Report the blood film (3 marks)

Normal platelets
Normal red cells
Normal white cells
Large, extracellular parasites present with an undulating membrane and flagellum.

b. Provide a preferred diagnosis, or differential diagnosis (2 marks)

Human African trypanosomiasis
(Two types: brucie gambiense (97% of cases) and brucei rhodeiense, not readily distinguishable by morphology. 70% of cases in last 5 years occurred in DRC.)

c. How is this illness transmitted? (2 marks)

Tsetse fly bites
(Also reported: placental transfer, sexual contact, needlestick injury)

Reference: Trypanosomiasis, human African (sleeping sickness) (who.int)

Question 11. A 55-year-old man presents to the emergency department with sudden onset confusion, right arm weakness and visual disturbance. He has no past medical history. A CT head demonstrates an acute cerebral infarct.

a. Report the blood film (3 marks)

Thrombocytopenia
Red cell fragmentation / schistocytes
Normal white cells

b. List five additional urgent tests would you request (5 marks)

ECG
Coag screen (PT/APTT/FGN)
Creatinine / U&E
Troponin / Pro-BNP
Pregnancy Test
ADAMTS13
Retic / Hapto / LDH / DAT

(Less time sensitive but relevant Ix to consider: HIV, Hep B, Hep C, Autoantibody screen, Echo, tumour markers, staging CT)

c. List five causes of these blood film appearances (5 marks)

TTP – Acquired or congenital
Pregnancy – HELLP, Eclampasia, AFLP
HUS – Acquired or congenital
Drugs – Qunine, tacrolimus, simvastatin, interferon, OCP, trimethoprim, gemcitabine, bleomycin have all been implicated
Malignant hypertension
Malignancy – adenocarcinoma
Post-allogeneic stem cell transplant
Infection – CMV, Adeno, Herpes simplex, Hep B, Hep C, Meningococcus, Fungal, HIV
Autoimmune – lupus nephritis, scleroderma, Evans, Vasculitis
Catastrophic antiphospholipid syndrome
Pancreatitis