



Higher Specialist Diploma

Immunology

September 2024

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.

Your colleague has asked you to help them interpret a set of Tryptase results. Explain what the following two sets of results show, including the possible diagnoses, and the further tests that could be performed to confirm this.

Serum Tryptase reference range: 2 - 14 ug/L

Case 1

Patient A presented to Emergency Department on the 1st of June with a widespread rash, shortness of breath, fall in blood pressure and loss of consciousness. Family member said they have been eating nuts.

Date	01/06/2023 (1pm)	01/06/2023 (4pm)	06/06/2023
Result	54 ug/L	39 ug/L	10 ug/L

Case 2

Patient B was referred to immunology clinic for 'allergy testing' due to recurrent symptoms of widespread rash, shortness of breath, and dizziness.

Date	30/12/2023 (1pm)	30/12/2023 (5pm)	03/02/2024	06/02/2024
Result	62 ug/L	56 ug/L	26 ug/L	28 ug/L

2.

Your laboratory has recently changed its primary testing strategy from ANCA (Immunofluorescence) testing to a solid phase screen (MPO/PR3) screen. You have been asked to present at the Renal and Rheumatology forum to explain the change. Describe the key points you need to explain in your presentation.

3.

You have been asked to discuss three sets of results on three different patients who have presented with the same symptoms to one of your trainee scientists. All three patients (patients C, D and E) presented with repeat episodes of abdominal cramping without obvious cause and swelling in the hands, lips and around the eyes, tongue, throat, or genitals. There was no common trigger. Patient C had onset following a tooth extraction, Patient D following a stressful episode and Patient E following a heavy cold.

Discuss the interpretation of the results and possible diagnoses to your trainee.

Patient C	Result	Reference Range
Complement C3	0.83 g/L	(0.75 - 1.65)
Complement C4	0.10 g/L	(0.14 - 0.54)
C1 esterase inhibitor (Level)	63 mg/L	(150 - 350)
C1 esterase inhibitor (Function)	19%	(> 70)

Patient D	Result	Reference Range
Complement C3	0.83 g/L	(0.75 - 1.65)
Complement C4	0.10 g/L	(0.14 - 0.54)
C1 esterase inhibitor (Level)	323 mg/L	(150 - 350)
C1 esterase inhibitor (Function)	<8%	(> 70)

Patient E	Result	Reference Range
Complement C3	1.01 g/L	(0.75 - 1.65)
Complement C4	0.22 g/L	(0.14 - 0.54)
C1 esterase inhibitor (Level)	254 mg/L	(150 - 350)
C1 esterase inhibitor (Function)	112%	(> 70)

4.

Lymphocyte subsets were tested on two patients, F and G, and the results are below. Reference ranges are also provided. Both patients are male, aged 65. No clinical details are provided for either patient. Reference ranges:

Population	Cells / uL
CD3+ T cells	690 - 2540
CD19+ B cells	90 - 660
CD4+ T cells	410 - 1590
CD8+ T cells	190 - 1140
CD16/CD56+ NK cells	90 - 590
CD4/CD8 Ratio	1.0 - 3.6

- 4a. Discuss any abnormal results, possible causes and further actions that may be required for Patient F. (10 marks)

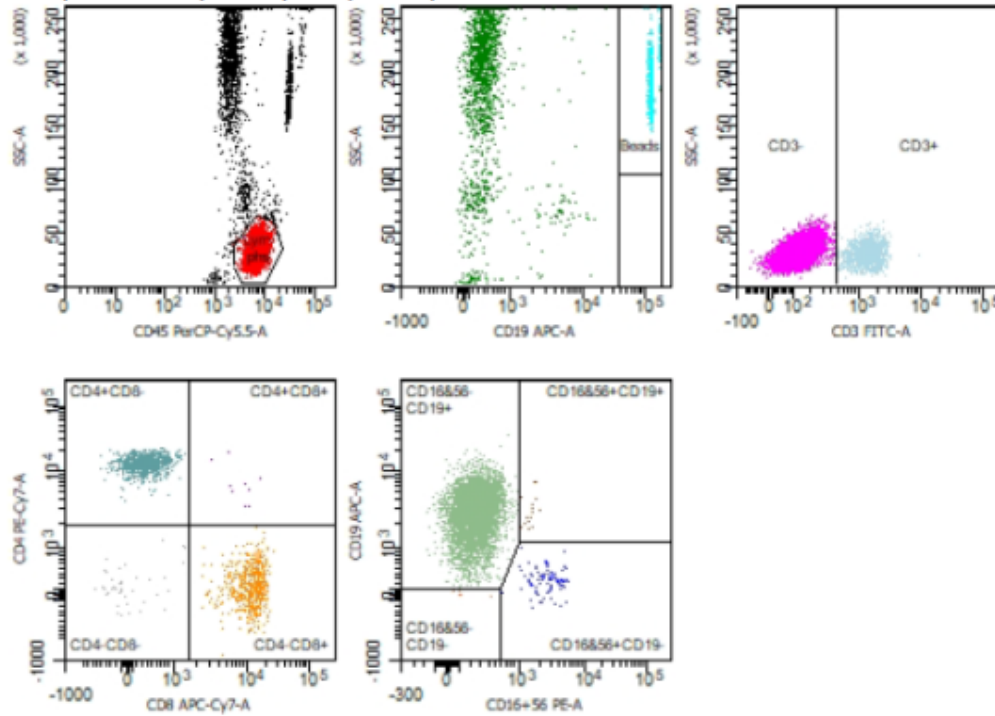
Patient F

QC Messages

Manual Gate is in effect.
% T-Sum is: 8.36
Lymphosum is: 99.69
4/8 ratio is: 0.06

CD3/CD16+56/CD45/CD4/CD19/CD8 TruC

Total Events: 10115



6 COLOUR001.001.fcs

Reagent Lot ID: 00000

Parameter	Percent	Value/AbsCnt
Lymph Events		7334
Bead Events		717
CD3+	18.82	1788.03
CD3+CD8+	7.14	678.93
CD3+CD4+	11.25	1068.93
CD3+CD4+CD8+	0.12	11.66
CD16+CD56+	1.10	104.95
CD19+	79.74	7577.12
CD45+		9502.49
4/8 Ratio		1.57

- 4b. Discuss any abnormal results, possible causes and further actions that may be required for Patient G. (10 marks)

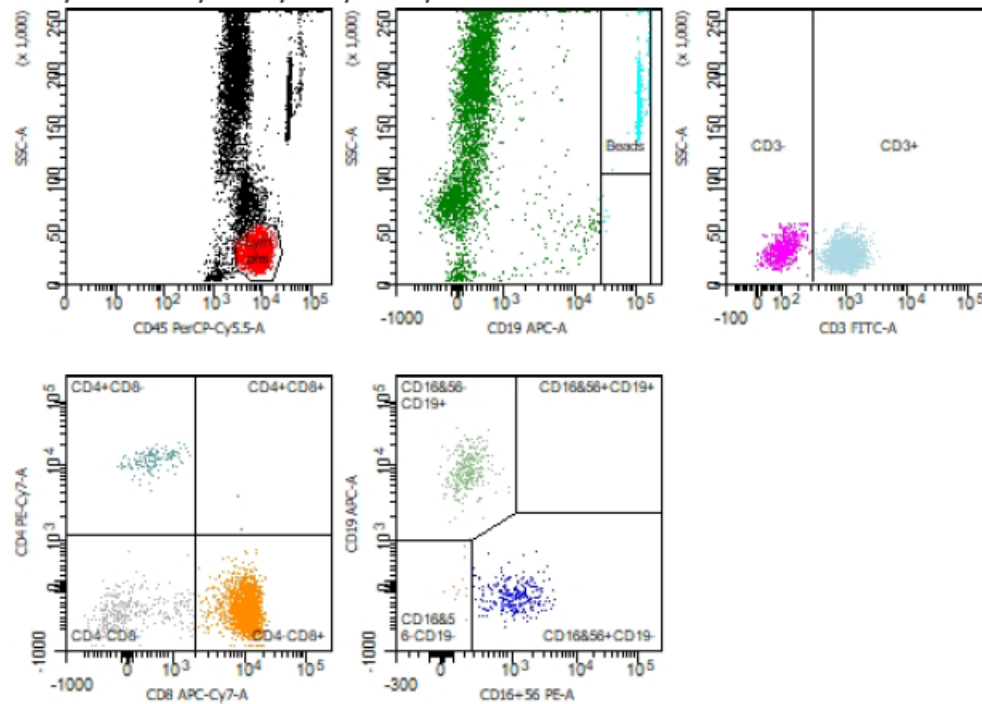
Patient G:

QC Messages

Manual Gate is in effect.
% T-Sum is: 0.42
Lymphosum is: 99.66
4/8 ratio is: 1.57

CD3/CD16+56/CD45/CD4/CD19/CD8 TruC

Total Events: 10045



6 COLOUR_a001.001.fcs

Reagent Lot ID: 00000

Parameter	Percent	Value/AbsCnt
Lymph Events		3515
Bead Events		1598
CD3+	83.53	1706.85
CD3+CD8+	71.07	1452.22
CD3+CD4+	4.10	83.71
CD3+CD4+CD8+	0.11	2.33
CD16+CD56+	7.65	156.38
CD19+	8.51	173.82
CD45+		2043.45
4/8 Ratio		0.06

4c. Describe the quality control of lymphocyte subsets.

(5 marks)



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Essay Paper

120 minutes

Attempt 2 out of 5 questions

Instructions to Candidates

1. Record your candidate number and HSD discipline on the front sheet of the answer booklet.
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3. Begin each new question on a new page.
4. Each question is worth 100 marks.

1. Critically appraise different approaches for the investigation of Autoimmune Blistering Diseases [AIBD].
2. Discuss the clinical utility of molecular allergology in diagnosis and therapy of allergic disease.
3. Discuss the challenges surrounding the quality assurance of functional cellular assays in the diagnostic laboratory.
4. Critically appraise current guidelines for minimum re-test intervals and demand management in immunology.
5. Describe, with examples, the immunoglobulin profiles you would expect to see in a range of immunodeficiencies.



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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.

A 12-year-old girl presents with severe pneumonia caused by *Streptococcus pneumoniae*. There is a history of repeated ear and sino-pulmonary infections and one incidence of autoimmune thrombocytopenia successfully treated with glucocorticoids. They are referred to immunology for further investigations.

Of note, the patient's father suffers recurrent chest infections and has bronchiectasis and her paternal grandmother died from lymphoma.

Blood results are as follows. A blood sample was collected for immunological analyses and the results obtained were:

	Patient Results	Reference Range
IgG	1.6 g/L	5.4 – 16.1 g/L
IgA	0.42 g/L	0.80 – 2.80 g/L
IgM	2.58 g/L	0.52 - 2.63 g/L
Tetanus antibody	0.07 IU/mL	0.1 – 10 IU/mL
Pneumococcal antibody	9 mg/mL	20 – 200 mg/L

	Patient Results (cells / uL)	Reference Range (cells / uL)
CD3+ T cells	590	800 - 3500
CD4+ T cells	180	400 - 2100
CD8+ T cells	610	200 - 1200
CD19+ B cells	150	200 - 600
CD16/CD56+ NK cells	124	70 - 1200
CD4/CD8 Ratio	0.3	0.9 - 3.4
Naïve T cells (CD45RA+)	118	>700
Activated / Memory T cells (CD45RA-)	640	<200
Regulatory T cells	Reduced	N/A

Extended B cell phenotype was performed at a referral hospital and reported as:

“Naïve B cells appear reduced in proportion to the total B cell population. Memory and class switched memory are within the reference range for the patient. Of note, transitional B cells are expanded and represent the majority of the B cells present.”

- a. What is the differential diagnosis? Consider three possibilities and discuss which is the most likely? (50 marks)

- b. Suggest a possible contributory gene mutation and discuss the underlying mechanism. (30 marks)
- c. With reference to this mechanism explain what are the possible treatment options? (20 marks)

UNSEEN CASE STUDIES

2.

A 58-year-old lady presented with gradually increasing tiredness, exertional dyspnoea and ankle swelling. For several months she had self-treated with oral iron and multi-vitamins without symptomatic improvement. She had lost weight, but denied any history of anorexia, dyspepsia or blood loss. On examination, she was pale and slightly jaundiced.

Laboratory investigation showed:

Haemoglobin	7.7g/dL	(reference range 12.0 – 16.0)
White cell count	$5.6 \times 10^9/L$	(reference range 4.0 – 11.0)
Platelets	$170 \times 10^9/L$	(reference range 150 – 400)
Serum vitamin B12	50 ng/L	(reference range 170-900)

Serum folate, serum iron and total iron-binding capacity were normal.

A blood film showed marked macrocytosis with a mean cell volume of 120fL (reference range 80 - 100fL) and bone marrow examination revealed marked megaloblastic erythropoiesis with abundant iron stores.

Antibodies to thyroid peroxidase were positive, although the patient was clinically and biochemically euthyroid.

- a. What is the likely diagnosis? Give your reasons. (20 marks)
- b. What further immunology serological tests would be indicated? (10 marks)
- c. Discuss the relative sensitivities and specificities of the serological tests you have identified in b. above. (30 marks)
- d. Discuss the treatment available for this condition. (20 marks)
- e. Discuss the relevance of the current guidelines for this condition in the light of the serological diagnosis. (20 marks)

3.

A 21-year-old man visited the accident and emergency room complaining of fever and headache that had lasted for two days, accompanied by nausea and vomiting. He had a petechial rash on both legs, hands, and the trunk, which appeared the day before the visit. He was a trainee policeman and had finished a 4-week training course 20 days before symptom onset. He had been vaccinated with a quadrivalent meningococcal conjugate vaccine. There was no past medical history.

Laboratory analysis showed elevated inflammatory parameters

CRP 360 mg/L [Reference range <5 mg/L]

Neutrophils $11.3 \times 10^3/\mu\text{L}$ [Reference range $1.5\text{--}5.7 \times 10^3/\mu\text{L}$]

Blood cultures revealed *Neisseria meningitidis* serogroup B, and a CSF culture revealed no microorganisms. He was treated with intravenous ceftriaxone (4 g/day) for 9 days and showed a good clinical response.

After six months, he revisited the accident and emergency room complaining of fever and headache accompanied by nausea and vomiting. He also reported upper respiratory symptoms, cough, and sore throat. Blood culture revealed *N meningitidis* again; however, it was not identified in the CSF culture. The microorganism isolated in this second event of *meningococemia* was also identified as serogroup B.

- a. What is the likely diagnosis? (20 marks)
- b. Due to the recurrent infection which immunology tests would you recommend? (20 marks)
- c. Which follow up tests would you request to confirm the results from the tests you have mentioned in part b? (20 marks)
- d. Critically appraise the technologies available for functional assays related to this group of diseases. (30 marks)
- e. Which prophylactic treatment would be advised for this patient? (10 marks)